

MENTHOL MOUTH SWILLING AND ENDURANCE RUNNING PERFORMANCE IN THE HEAT

RUSSELL BEST

School of Health and Social Care
Teesside University, Middlesbrough, UK

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Abstract

Heat challenges multiple physiological systems, and its effects are heavily felt by endurance athletes due to the duration and intensity that must be sustained in competition and training sessions. Runners may demonstrate impaired thermoregulatory responses or opportunities due to lower rates of convective cooling and fewer opportunities to provide cooling interventions during exercise than other endurance athletes e.g. cyclists. Cooling strategies may be employed before or during exercise to minimise the effects of heat exposure, and their effects have been studied for at least three Olympic cycles. Hence, the optimisation of timing and method of delivery of cooling provision, with the addition of any novel strategies, would be of benefit to the contemporary sport and exercise science practitioner.

Initially this thesis sought to better understand the effects of cooling strategies upon time trial performance in endurance sports with a systematic review and meta-analysis. The efficacy of strategies was assessed with respect to intervention timing (pre or per-cooling or both) and method of delivery (oral or topical or both). Cooling strategies were found to provide small but ecologically relevant improvements in time trial performance, especially when administered during the exercise bout to the oral cavity; the addition of menthol was seen to possibly enhance ergogenic effects. Hence, a second systematic review regarding external or internal application of menthol was conducted and found that menthol demonstrated improvements in performance when applied internally, most likely due to altered thermal and ventilatory responses.

A range in menthol concentrations and dilution methods was noted in the literature, establishing a clear need for a randomised trial to ascertain menthol concentration preference. Following appropriate dilution, 0.1% menthol was determined to be preferred; colour preference was also established to maximise the perceptual cooling effect of menthol solution. This solution was then used (without colour to ensure blindness) in subsequent investigations. At rest this solution was shown to improve perceptions of thermal comfort, thermal sensation and thirst, when compared to carbohydrate and water swilling.

Two exercise trials were conducted: the first examined the effects of menthol mouth swilling upon physiological and perceptual markers over four minute intervals at a range of pertinent running speeds (14-20km.h⁻¹), and following 1km time trial performance. Effects on time trial performance were unclear, as were the effects in physiological parameters. Thermal comfort however was improved, with menthol mouth swilling counterintuitively increasing thermal sensation and thirst in the heat (35°C), but

ameliorating these factors in the cold (15°C). Secondly, at a fixed rating of perceived exertion, corresponding to 2mmol.L⁻¹ blood lactate, runners demonstrated a lower oxygen consumption following menthol mouth swilling for the latter two thirds of a 30-minute training session than compared to no swill or ice swilling. No changes in ventilation were shown, and the perceptual responses at a group level were unclear – suggesting that whilst menthol may improve the oxygen cost of running at a fixed rating of perceived exertion, this does not correspond to improvements in thermoregulatory perception in this sample. Qualitative responses regarding the swill from the athletes involved in the exercise studies were collated and menthol was considered an enjoyable and useful strategy by the athletes. Further research is required to assess if these hedonic and utilitarian perspectives are rated as highly in more ecologically valid environments; the athletes indicated this would be the case.

The findings presented in this thesis demonstrate that a light blue or light green 0.1% menthol mouth rinse is preferred and can alleviate thermal sensation and thirst, and improve thermal comfort at rest in the heat. During exercise in a small sample of trained distance runners, menthol mouth swilling may alleviate perceptual symptoms of heat exposure without necessarily improving performance, dependent upon the running speeds chosen. Furthermore, menthol mouth swilling is considered a pleasant and potentially ergogenic strategy by athletes who have used it, suggesting that even in the absence of performance or physiological enhancements that exceed the typical coefficient of variation in performance, menthol mouth swilling is a viable nutritional support strategy for trained distance runners, when exercising in the heat.

Scientific Output

Conference communications

Best, R. What's new in mouth rinse nutrition: Update on fluid and menthol. International Sport and Exercise Nutrition Conference (ISENC). Newcastle upon Tyne, United Kingdom. December 2018. Oral Presentation.

Best, R. and Berger, N.J.A. Menthol mouth rinsing evokes mixed responses in trained runners. Sport and Exercise Science New Zealand (SESNZ). Cambridge, New Zealand. October 2017. Oral presentation.

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List of abbreviations

BMI	Body mass index
CL	Confidence limit
dRPE	Differential rating of perceived exertion
FFM	Fat free mass
HR	Heart rate
HR _{max}	Maximum heart rate
HR _{peak}	Peak heart rate
LT	Lactate threshold
PEDro	Physiotherapy evidence database
RE	Running economy
RPE	Rating of perceived exertion
RPE _{legs}	Rating of perceived exertion at the legs
RPE _{lung}	Rating of perceived exertion at the lungs
RPE _{over}	Overall rating of perceived exertion (gestalt interpretation)
S.D.	Standard deviation
T _{core}	Core temperature
T _{rec}	Rectal temperature
T _{skin}	Skin temperature
T _{tymp}	Tympanic temperature
TC	Thermal Comfort
TRP	Transient receptor potential
TRPM8	Transient receptor potential melastatin eight
TRPV1	Transient receptor potential vanilloid one
TS	Thermal sensation
VAS	Visual analogue scale
$\dot{V}O_2$	Oxygen uptake
$\dot{V}O_{2max}$	Maximal oxygen uptake
$\dot{V}O_{2peak}$	Peak oxygen uptake
$v \dot{V}O_{2max}$	Velocity at which maximal oxygen uptake occurs

Authorship contributions

Authors and their contributions to each chapter within this thesis and its published works, where the candidate is the sole author of the chapter, no clarification as to contribution is provided.

Chapter	Title	Author(s) and Contribution(s)				
1	Introduction	Russ Best				
2	Literature Review	Russ Best				
3	Topical and Ingested Cooling Methodologies for Endurance Exercise Performance in the Heat (Meta-Analysis)	Russ Best	Stephen Payton	Iain Spears	Florence Riera	Nicolas Berger
		Lead author; literature search strategy and execution; meta-analyses	Co-author; literature search corroboration	Co-author; manuscript finalisation	Co-author; manuscript finalisation	Co-author; manuscript preparation
4	Menthol: A fresh ergogenic aid for athletic performance (Systematic Review)	Christopher Stevens		Russ Best		
		Methods; Topical Application of Menthol sections; collaboration for concluding sections		Introduction; Oral Application of Menthol sections; collaboration for concluding sections		
5	The Development of a Menthol Solution for use during Sport and Exercise	Russ Best	Iain Spears	Philip Hurst	Nicolas Berger	
		Lead author; study design; menthol dilution and administration; statistics	Co-author; manuscript preparation	Co-author; placebo consultant; manuscript preparation	Co-author; study design; manuscript preparation	
6	Perceptual and Physiological Responses to Carbohydrate and Menthol mouth-swilling solutions	Russ Best	Peter Maulder		Nicolas Berger	
		Lead author; study design; menthol dilution and administration; statistics	Co-author; statistical guidance; manuscript finalisation		Co-author; manuscript preparation and finalisation	
7	Menthol Mouth swilling and Running Performance at Different Intensities and Temperatures	Russ Best				
8	Swilling of Physiological or Perceptual Cooling Agents during a Simulated Running Training Session in the Heat	Russ Best				
9	Athlete Evaluations of Menthol Mouth Swilling	Russ Best				
10	Synthesis of Findings	Russ Best				

CHAPTER 1 : INTRODUCTION

1.1 Overview

Heat is broadly considered deleterious to endurance exercise performance. This is because heat exacerbates physiological symptoms across multiple systems, that are contributory to fatigue (Périard, Racinais and Sawka, 2015; Racinais *et al.*, 2015). The worsening of these symptoms may also impose perceptual challenges to the exercising athlete, which may also accelerate the onset of fatigue, volitional exhaustion or withdrawal from exercise. Heat challenges an athlete's convective, evaporative and radiant cooling mechanisms, whereas cooling via conduction is unlikely during exercise performance. These impairments can be worsened by factors such as clothing choice, humidity, solar radiation, time of day and athlete and wind velocities (Maughan, 2010; Otani *et al.*, 2016; 2017; Shimazaki, Yoshida and Yamamoto, 2015). Failure to minimise these effects increases the rate of heat storage experienced by an athlete, elevating core temperature and stressing cardiovascular, respiratory and sudomotor systems (Périard *et al.*, 2015), hereby increasing the rate at which fatigue is experienced.

Exercise performance in the heat is a contemporary and relevant topic for sport and exercise practitioners and scientists, not only due to elevated global temperatures as a result of global warming, but primarily because of the awarding of multiple major sporting tournaments to countries with high ambient temperatures (Gerrett *et al.*, 2019) e.g. Commonwealth Games 2018, Gold Coast, Australia; Rugby World Cup 2019 and Olympics 2020 Tokyo, Japan; FIFA World Cup Qatar 2022. Therefore, strategies to minimise the effects of heat upon exercise performance are of international sporting importance, and the failure to do so will directly affect nations' performances, recovery and medal counts at these pinnacle events.

Each sport, due to variations in performance time, intensity and regulations, possesses a 'heat storage fingerprint', which restricts the strategies that can be employed to cool athletes. For instance, it is unlikely that a sailor would employ the same cooling strategy as an equestrian due to their markedly different event environments, scoring criteria and time pressures. Hence a variety of strategies have been developed and investigated that can be broadly categorised via timing (pre or per-cooling) and type (ingested or topical; Best, Payton *et al.*, 2018), and may be further classified by their mechanism of cooling, being either perceptual or physiological in nature. This presents the athlete, practitioner or sports scientist with a web of cooling strategies that can be employed, but practicalities

must always be considered, ultimately asking ‘What limits performance for this athlete in the heat and how can this be mitigated within the practical and regulatory constraints?’.

The benefits of cooling strategies may extend beyond the physiological symptoms of a lower core or skin temperature. Recently, there has been growing interest in ameliorating the perceptual effects of exercising in the heat, which typically present as an increased thermal sensation and decreased thermal comfort (Flouris and Schaller, 2015). One such strategy is menthol application before and/or during exercise (Stevens and Best, 2017; Chapter 4). Menthol evokes feelings of cooling and freshness that are familiar to most cultures through confectionary or oral hygiene products, but may also be present in products used to treat muscular injury (Galeotti et al., 2002; Gaudio et al., 2012), and has historically been used in respiratory medicine since at least the late 19th century (Potter, 1890; Somers, 1896), following its characterisation in the mid-19th century (Oppenheim, 1861;1862).

Menthol has been applied topically during exercise, with little ergogenic effect seen following a single application (Gillis, House and Tipton, 2010; Barwood, Corbett and White, 2014; Gillis, Weston, House and Tipton, 2015) but may be beneficial if this applied repeatedly throughout the exercise bout (Barwood *et al.*, 2018). Oral application of menthol via a mouth rinse however, has shown promise in runners (Stevens, Bennett, et al., 2016; Stevens, Thoseby, et al., 2016) and cyclists (Jeffries *et al.*, 2018; Flood *et al.*, 2017; Mündel and Jones, 2009) and offers a method of menthol application that is easy to administer and more readily employed during exercise than a menthol cream or spray. Research assessing oral application of menthol upon time trial performance has to date focused exclusively in runners (Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016), with athletes reporting 5km times of approximately 20-minutes or slower. Whilst this suggests menthol mouth swilling may alleviate perceptual heat symptoms and improve performance in recreational runners, there is a clear need to assess the efficacy of menthol mouth swilling in faster runners, who may display improved thermoregulatory abilities. Assessment of the product at a range of race specific intensities and training sessions is also warranted.

1.2 Purpose of the research

The primary aim of this thesis was to develop a novel mentholated solution to be administered as a perceptual cooling strategy for use during endurance exercise performance. This strategy was administered to trained middle and long distance runners

at competitive and training intensities and its effects compared to that of other ergogenic strategies, in hot environmental conditions.

Specifically, this thesis aimed to determine the preferred concentration of menthol within a mouth swill, to be employed during subsequent studies (Chapter 5). Preferred colour was also assessed, with a view to producing a product for application outside of a controlled laboratory environment that maximised sensory cooling characteristics. This solution was then used in a series of investigations.

Firstly, the physiological and perceptual responses of the mentholated mouth swill were compared to a carbohydrate solution and control swill, at rest, in hot environmental conditions (Chapter 6). Two exercise trials followed this initial resting experiment: Trial one (Chapter 7) assessed the ventilatory, physiological, performance and perceptual responses to mentholated mouth swilling at typical training and competitive intensities, in temperatures pertinent to British middle and long distance runners. Whereas trial two (Chapter 8) compared the ventilatory, physiological and perceptual responses of ice and mentholated mouth swill during a 30-minute training session, at a fixed rating of perceived exertion, in the heat. These studies were conducted in tandem, to replicate a typical training cycle with a view to increasing participant recruitment and retention. There was a negligible crossover in participant recruitment between the solution development and trial performed at rest to minimise expectancy and experience of mentholated mouth swilling. Finally, qualitative responses and feedback on menthol mouth swilling during exercise and its potential for application outside of the laboratory in differing environmental conditions and at different exercise intensities were captured (Chapter 9).

1.3 Philosophical approach to the problem

Throughout this thesis, it will become clear that a stance is taken with respect to three key tenets of exercise performance in the heat, fatigue and the characterisation of athletes. These concepts are examined in the literature review, and revisited throughout the course of the experimental chapters but their introduction here outlines the philosophy which underpinned the work presented, and how this work was conducted.

Firstly, critical core temperature is considered a theoretical maximum temperature that can be sustained prior to the onset of (heat) exhaustion (Cheung and McLellan, 1998; González Alonso *et al.*, 1999; Nielsen *et al.*, 1993; 1997; Nybo and Nielsen, 2001). This assertion has been consistently challenged in the literature (Byrne *et al.*, 2006; Ely *et al.*, 2009), and may differ markedly between heat acclimation and training statuses (Cheung and McLellan, 1998; Racinais *et al.*, 2019). Increasingly evidence is presented from applied

investigations that demonstrate rectal temperatures $>40^{\circ}\text{C}$ with absence of heat illness symptoms (Racinais *et al.*, 2019; Stevens *personal communication*), suggesting that a high core temperature is a correlate of fatigue, and not the driver of fatigue *per se*. More likely is that it is an athlete's interpretation of the 'signal' of being hot, relative to other physiological and psychological 'noise' of exercise performance, that produces fatigue. Secondly and similarly, an interoceptive approach to fatigue is adopted throughout this thesis. Interoception can be defined as a homeostatic sense of 'How do I feel now?' (Craig 2002; 2009) from afferent physiological signals. This provides an established neurological framework that when applied to exercise, serves as a more complete model of fatigue than the Central Governor model, or purely physiological causes. The former being largely teleological, the latter perhaps too reductionist. Thirdly, the language used to characterise the training statuses of individuals in experiments is often ambiguous and/ or loaded. For instance, 'untrained' and 'trained' are frequently used in the literature but may not be operationalised. This issue is further complicated by adjectives such that 'recreationally-trained' or 'well-trained' may obfuscate and not elucidate the reader's interpretation of participants' fitness. Empirically defined training statuses, linked to physiological landmarks are more useful and are established for cyclists (De Pauw and Roelands, 2013), and to a lesser extent runners (Barnes and Kilding, 2015). Stratifying athletes by performance time is another method of classification; whilst one cannot necessarily label athletes by performance time, they provide a meaningful interpretation of physiological and performance capabilities – ultimately it is an athlete's capability to realise physiological limits that elicits medal winning performances at major championships.

1.4 Potential Impact

This thesis adds to the body of literature concerning cooling athletes when performing in the heat. Perceptual cooling is a recent addition to this field, with the majority of prior research assessing physiological cooling strategies, employed before or during exercise. Despite menthol's ability to impart feelings of cool and freshness being known since the late 19th century, recent use in sport and exercise has focused upon topical menthol application. However, this has shown limited efficacy and may even be deleterious with respect to thermoregulation, whereas the oral application of menthol has shown predominantly positive effects thus far, albeit in recreationally trained athletes, and presents a more practically viable strategy for menthol use during exercise. Therefore, this thesis is the first attempt to assess the effects of menthol mouth swilling in competitive

athletes that represent an empirically defined ‘well-trained’ group. This novelty is extended by examining a range of training and competition running speeds (Chapter 7) and assessing menthol’s efficacy in a typical training session (Chapter 8), emphasising the importance of trialling and establishing the effects of sports nutrition strategies in training, prior to use in competition (Maughan *et al.*, 2018). Qualitative feedback is also included to support these findings (Chapter 9).

The findings of this thesis have the potential to encourage commercial production of a mentholated beverage or swill for use during exercise in hot conditions, or potentially for those that suffer from dyspnoea, or more generally people who enjoy the oral cooling sensation of menthol. The commercial value of such a product is unknown, but is certainly pertinent with increasing global temperatures, and an increasing percentage of major sporting events being held in locations where ambient temperatures are either hot all year around, or will be hot at the time of major events.

CHAPTER 2 : REVIEW OF THE LITERATURE

2.1 Heat as an applied problem for athletes

Professional endurance sports are subject to an increasingly demanding global calendar; athletes must traverse continents, time zones and differing thermic environments, often in quick succession and with little to no time for acclimatisation (Table 2.1). This problem is potentially compounded in multi-day events such as cycling's Grand Tours (Il Giro d'Italia, Le Tour de France & La Vuelta d'Espana), during which the climate may vary drastically daily, along with changes in course profiles, individual rider goals and teams' strategies. Runners too, are well documented in their struggle to combat the heat during endurance competitions. Anecdotal and experimental evidence documents the challenges faced by former marathon world record holder Alberto Salazar when preparing and competing in thermally challenging environments (Stracher, 2013; Armstrong, Hubbard, *et al.*, 2016), one such episode resulting in Salazar being read his last rites by a priest whilst submerged in an ice bath (Salazar and Brant, 2013; Stracher, 2013), akin to Pheidippedes after the battle of Marathon. All athletes are at the mercy of competitive organisation (or lack thereof) and regulations, provision of ingested and topical cooling strategies and the environment when competing in hot conditions. This chapter therefore will first describe the limiting factors of endurance performance and associated models of fatigue before detailing how heat is a fatiguing factor during endurance exercise and concluding with cooling strategies employed by athletes to limit the effects of heat on performance.

2.2 Limiting factors of endurance performance

Endurance performance is a complex, multi-factorial output driven by, and derived from multiple biological systems. Considerable debate exists within the literature as to whether fatigue is attributed exclusively to physiological, psychological and neurological factors via feed-forward and feedback mechanisms, or a combination of these systems. An understanding of these factors, under different conditions, is necessary to inform strategies implemented by athletes and practitioners to combat fatigue. In this section, a classic multi-factorial model (Joyner and Coyle, 2008) is described before examining limiting factors individually (Sections 2.2.1-2.2.3), and categorising them in a more contemporary fashion (Section 2.3), before outlining the challenges posed by exercise in the heat (Section 2.4) and strategies to combat these (Section 2.5).

In their topical review, examining the physiology of champions, Joyner and Coyle (2008) proposed a schematic model of endurance performance that sought to explain the performance velocity or power output attained and sustained throughout a competition as an expression of performance $\dot{V}O_2$ plus performance O_2 deficit, multiplied by gross mechanical efficiency. Each of these broad, primary factors are made up of sub-factors which are products of morphological adaptations and constraints (Joyner and Coyle, 2008). More simply, this can be expressed as the difference between the aerobic or oxidative and the anaerobic or glycolytic contributions to exercise, whilst accounting for one's (bio)mechanical efficiency.

The aerobic contribution to performance (performance $\dot{V}O_2$) is a product of the $\dot{V}O_2$ at lactate threshold, which itself is a product of an athlete's maximal oxygen uptake ($\dot{V}O_{2max}$) (both explored in Section 2.3.2.1). A high $\dot{V}O_{2max}$ is considered a prerequisite for elite endurance performance. However, improvements in this parameter may contribute significantly more to short endurance events such as the 1500m than over longer events such as a marathon, where one's capacity to exercise at a high percentage of $\dot{V}O_{2max}$ over a prolonged duration is considered more important (D. W. Hill, 1999; Spencer and Gastin, 2001; Duffield, Dawson and Goodman, 2005; 2007). The ability to sustain a high fractional utilisation of $\dot{V}O_{2max}$ without the accumulation of lactate within the blood is the $\dot{V}O_2$ at lactate threshold (Joyner *et al.*, 2020; Joyner and Coyle, 2008), with the $\dot{V}O_2$ of submaximal but pertinent running speeds considered an athlete's running economy (Joyner *et al.*, 2020; Saunders, Pyne *et al.*, 2004; see Section 2.3.2.1 for further discussion). The mechanistic underpinnings of performance $\dot{V}O_2$ are predominantly cardiovascular and haematological, for example stroke volume and haemoglobin concentration (Joyner and Coyle, 2008), although intramuscular changes in factors such as capillary density and enzyme concentrations also encourage aerobic metabolism (see sections 2.2.1.2 and 2.2.1.4 for further detail).

Similarly, enzymatic factors and the distribution of resources and effort during the exercise bout can affect performance $\dot{V}O_2$ and performance O_2 deficit. Increases in exercise intensity, possibly due to poor pace management, will increase performance $\dot{V}O_2$ and ultimately facilitate a performance O_2 deficit. This transition will result in a greater oxidation of glycogen (see 2.2.1.4) and a concomitant increase in blood lactate accumulation, and dissociated H^+ and P^+ ions (Kent *et al.*, 2016). This metabolic milieu may limit muscle contractility (Section 2.2.1.1) and thus hamper performance. This unfavourable intramuscular condition may be attenuated by endogenous or exogenous

buffers such as sodium bicarbonate (NaHCO_3), sodium citrate ($\text{Na}_3\text{C}_6\text{H}_5\text{O}_7$) or beta-alanine ($\text{C}_3\text{H}_7\text{NO}_2$; R.L. Jones *et al.*, 2016; Russell *et al.*, 2014; Sale *et al.*, 2011).

Finally, the performance $\dot{V}\text{O}_2$ and performance O_2 deficit manifest as a product of an athlete's mechanical efficiency, which relies upon the phenotypic qualities and muscle fibre type preponderance of the athlete (Joyner and Coyle, 2008). Phenotypic adaptations are discussed in section 2.3.2.2, although it should be noted that with respect to running economy (i.e. performance $\dot{V}\text{O}_2$) alterations in bodyweight may explain up to 94% of variance within the measure (Lundby *et al.*, 2017). With respect to muscle fibre type, Type I muscle fibres are considered more energetically efficient (Joyner and Coyle, 2008) than Type II fibres, but the relationship between muscle fibre type and running economy (and thus performance) is complicated by the mechanical complexity of running and an individual's morphological and biomechanical constraints (Joyner and Coyle, 2008; Williams, 2007). Whilst complex, running economy can be improved in a relatively short time frame through appropriate loading of elastic tissues via plyometric and resistance training (Denedai *et al.*, 2017) and chronically to high mileage endurance training (Jones, 2006).

The following sub-sections outline other physiological, psychological and environmental factors, not necessarily covered by Joyner and Coyle's (2008) review, which contribute to fatigue. This examination of fatigue is then extended by describing other models of fatigue with particular reference to endurance performance (Section 2.3).

2.2.1 Physiological

2.2.1.1 Central Nervous System and Neuromuscular activation

This section will introduce the role of the central nervous system and resultant neuromuscular activation as an explanation for fatigue during endurance performance. Information regarding how heat can affect these outcomes is noted in section 2.4.1.1. However, information pertaining to neurochemical theories of central fatigue are not included in either section to avoid deviation from the scope of the thesis, but have been concisely reviewed by McMorris and colleagues (McMorris, Barwood and Corbett, 2018). For the purposes of this literature review, central drivers of fatigue are considered factors which occur proximal to the neuromuscular junction (Carroll, Taylor and Gandevia, 2017) including the brain stem and spine; pertinent factors that present in the muscle i.e. distal to the neuromuscular junction are considered separately in section 2.2.1.2.

Evidence for central factors as drivers of fatigue is predominantly presented in the form of that obtained following maximal voluntary contractions (MVC), or episodic maximal

contractions inserted within a submaximal or locomotor exercise bout (Carroll, Taylor and Gandevia, 2017). The assessment of central contributions to fatigue is complicated during locomotor activities due to time required to instrument participants potentially invalidating findings (Carroll, Taylor and Gandevia, 2017), and in sports such as running, eccentric contractions (Martin *et al.*, 2004; G. Y. Millet, Tomazin, *et al.*, 2011; G. Y. Millet, 2011) further compound this issue as eccentric activity can longitudinally decrease voluntary activation of damaged musculature (G. Y. Millet, Tomazin, *et al.*, 2011).

Despite this as exercise duration increases, a reduction in central drive is observed (Lepers *et al.*, 2002; Tucker *et al.*, 2004; E. Z. Ross *et al.*, 2007; E. Z. Ross, Gregson, *et al.*, 2010; E. Z. Ross, Goodall, *et al.*, 2010). Similar effects are seen in sustained submaximal contractions, as measured by electromyography (EMG). A reduction in the ability to sustain a muscle contraction diminishes as duration increases, but is also associated with an increase in perception of effort (Lepers *et al.*, 2002; Tucker *et al.*, 2004), suggesting a partial role of central factors to endurance fatigue. An increase in motor unit recruitment as voluntary contraction duration increases is also seen, and corroborated by work that demonstrates a reduced contribution of central factors in sustained low-percentage contractions as load increases (Carroll, Taylor and Gandevia, 2017). This appears counterintuitive from a ‘below the neck’ perspective, as one would anticipate that as contraction/exercise duration increases there would be an increased contribution of peripheral factors to fatigue. Indeed, both may be true. The increased recruitment of motor units seen with low-percentage contractions imposes a greater central cost, but factors such as glycogen depletion and the accumulation of H⁺ and P_i ions within the muscle may also work to limit contractility (Kent *et al.*, 2016) and increase perception of effort during sustained low-percentage contractions. These effects are also noted in lower-limb musculature not associated with the task, termed non-local muscle fatigue (Halperin, D. W. Chapman and Behm, 2015), suggesting central factors may both be contributing to and preventing fatigue, simultaneously, dependent upon muscle group recruited (Halperin, D. W. Chapman and Behm, 2015).

A final consideration with respect to endurance performance is the rate of recovery of central factors following exhaustive endurance exercise. Given the threat to ecological validity imposed by the assessment of MVC during acute interventions noted above, studies that assess the time course of central responses hours-days after an endurance event potentially provide more meaningful data upon the cumulative effect of endurance exercise upon central factors, potentially supporting explanations of phenomena such as non-functional overreaching/ overtraining (Wijnberg *et al.*, 2008) or relative energy

deficiency (Mountjoy *et al.*, 2014; 2015), and informing recovery and training strategies post-event. Emma Ross demonstrates that neuromuscular factors are acutely impaired following a marathon demonstrate a relatively short rate of recovery within two days (E. Z. Ross *et al.*, 2007). Ross adds to this with a study that simulated participation in Le Tour de France (E. Z. Ross, Gregson, *et al.*, 2010) and found that although MVC values returned to baseline within two days, voluntary activation and motor evoked potential were inhibited from day 9 of the tour and remained suppressed beyond the conclusion of the study (E. Z. Ross, Gregson, *et al.*, 2010). Millet and colleagues (G. Y. Millet, Tomazin, *et al.*, 2011) extended the assessment timeline to 16 days following a 166km ‘extreme mountain ultra-marathon’ (positive and negative elevation: 9500m) and participants’ values of EMG and force production data took nine and 16 days to return to baseline, respectively. For comparison, changes in blood borne markers of muscle damage demonstrated a faster recovery rate of five to nine days (G. Y. Millet, Tomazin, *et al.*, 2011).

Central factors clearly cannot be ignored as a contributory factor to endurance exercise performance, but do not work in isolation. Whilst acute studies may limit direct transfer or ecological validity they provide a useful mechanistic snapshot of how fatigue is generated outside of the muscle, with the monitoring of these responses beyond exercise performance serving as useful indices of recovery.

2.2.1.2 Muscular efficiency

Exercise training proliferates changes within the muscle that are metabolically advantageous. These include, but are not limited to, increases in mitochondrial density, a more proximal location of substrate for mitochondria, enhanced enzymatic function and proliferation of enzymes corresponding to training metabolism/intensity. Muscle fibre type may also alter due to an exercise stimulus. Exercise alone may not drive intra-muscular changes; other external stimuli such as diet (Leckey *et al.*, 2006; D. M. Craig *et al.*, 2015) and environmental stress (O. R. Gibson *et al.*, 2017) may also ‘turn on’ the muscle to adapt. This section will provide a brief overview of mitochondrial and enzymatic adaptations to endurance exercise; mechanical and structural factors are discussed in section 2.3.2.2. Transcriptional factors are not discussed as much of this work is carried out in rodents who display different $\dot{V}O_2$ characteristics to humans (N. C. Gonzalez and Kuwahira, 2018), so limiting the contribution of such findings to the present discussion, although it is duly acknowledged that mitochondrial biogenesis is limited by transcriptional factors (Hood *et al.*, 2006; Hawley *et al.*, 2014).

Mitochondrial density increases with endurance exercise training (Vogt *et al.*, 2001; Montero *et al.*, 2015; Lundby and Jacobs, 2015; van der Zwaard *et al.*, 2016; MacInnis and Gibala, 2016); specifically, this adaptation occurs in two locations, increasing intermyofibrillar mitochondrial content (80%) and subsarcolemmal (20%) mitochondrial content (Hood *et al.*, 2006; Lundby and Jacobs, 2015), with greater mitochondrial content seen in Type I muscle fibres (Holloszy and Coyle, 1984; Schrauwen-Hinderling *et al.*, 2006; van der Zwaard *et al.*, 2016). Mitochondrial density may increase by up to 40% following exercise training (Montero *et al.*, 2015) and this increases the muscle's ability to function aerobically. Metabolically this means a greater rate of lipolysis is possible at a given exercise intensity (Holloszy and Coyle, 1984), with these adaptations observed after a single bout of exercise in rodents (Picard *et al.*, 2013), yet increased mitochondrial density is also associated with increased absolute and relative $\dot{V}O_{2\max}$ and skeletal muscle respiratory capacity (Lundby and Jacobs, 2015).

The proximity of substrates to the mitochondria also changes following exercise training. Lipids, stored as intramuscular triglycerides, demonstrate a meaningful contribution to prolonged exercise at lower intensities, diminishing in a fashion that parallels glycogen depletion in moderate to high intensity exercise. Intramuscular triglycerides, again like glycogen, increase after consistent exercise training (Schrauwen-Hinderling *et al.*, 2006), increasing as much as 2.5 times in trained athletes (Hoppeler *et al.*, 1973).

Mitochondrial function can be assessed through enzymatic activity associated with the respiratory capacity of the muscle (Lundby and Jacobs, 2015), whereas carbohydrate metabolism may be better assessed via pyruvate dehydrogenase (PDH) activity (Stellingwerff, 2005), due to preferential oxygenation during high intensity activity. A complete discussion is beyond the purpose of this section; however, it is noteworthy that oxidative phosphorylation capacity is associated with mitochondrial density and displays a response to training (Lundby and Jacobs, 2015; Montero *et al.*, 2015), as does succinyl dehydrogenase activity (van der Zwaard *et al.*, 2016). Nutritional manipulation may also modify enzymatic factors, for instance high fat feeding can impair glycogenolysis and decrease PDH (Stellingwerff, 2005), impairing high intensity exercise performance within the muscle. Such enzymatic reactions are an important consideration for the physiologist and associated athlete support staff as the impairment of exercise performance by enzymatic inhibition (Leckey *et al.*, 2006; Burke *et al.*, 2017) presents a clearly avoidable explanation for fatigue or underperformance, and further emphasises the trainability of the muscle at the molecular level.

2.2.1.3 Respiratory limits

Maximal oxygen uptake ($\dot{V}O_{2\max}$) and relative oxygen consumption i.e. exercise economy are discussed in Section 2.3.2.1, whereas this section will provide a brief discussion on $\dot{V}O_2$ kinetics and ventilatory threshold (VT) and their ability to limit or differentiate between levels of performance. Respiratory exchange ratio (RER). is discussed in the following sections as whilst it is calculated from respiratory parameters $\dot{V}CO_2$ and $\dot{V}O_2$, it is commonly used as an expression of substrate oxidation.

$\dot{V}O_2$ kinetics physiologically describe the transition from a resting state to that of metabolic activity with respect to oxygen consumption at the point of the muscle (in healthy individuals), as opposed to $\dot{V}O_{2\max}$ which may be limited by a range of upstream factors (Poole and A. M. Jones, 2012). This progression from resting to meeting the $\dot{V}O_2$ of an activity is primarily considered in exercise settings, however it also reflects spontaneous shifts in metabolic activity brought about by daily living activities such as climbing stairs, getting up from a chair or play in children. A standard $\dot{V}O_2$ kinetic curve is typically displayed in two parts: a fast component, and a slow component. The fast component occurs at the onset of exercise and is measured by the time constant, tau (τ) which may span a range of 10-100sec (Poole and A. M. Jones, 2012), and is a marker of how rapidly the demand of exercise is met i.e. how quickly one reaches a steady state of oxygen consumption ($\dot{V}O_{2ss}$). The slow component denotes a progressive increase in $\dot{V}O_2$ as exercise duration increases and is predominantly attributed to metabolic and mechanical changes within the exercising muscle, but factors such as $\dot{V}E$ and auxiliary muscular recruitment may also contribute to the increasing oxygen cost (Poole and A. M. Jones, 2012).

Faster kinetics (elevated τ) are considered beneficial, as this speeds the rate at which $\dot{V}O_2$ at the muscle matches the demand of exercise, and so are seen in trained endurance athletes (Kilding, Winter and Fysh, 2006; Kilding, Fysh and Winter, 2007) or animals such as greyhounds and horses (Poole and Erickson, 2011). Ergo, slower kinetics limit the rate at which one can respond to the demands of exercise and may be seen in lesser trained individuals, or those unable to meet the demands of exercise. Applied examples of $\dot{V}O_2$ kinetics include fast starts during a race which challenge the fast component (A. M. Jones *et al.*, 2007; Bailey *et al.*, 2016), training at intensities that elicit $\dot{V}O_{2\max}$ (Billat *et al.*, 2000) or the ventilatory threshold which both challenge the slow component and the use of high intensity exercise to prime $\dot{V}O_2$ kinetics (Ingham *et al.*, 2013). Based upon the evidence presented above, $\dot{V}O_2$ kinetics provide a limitation for endurance performance at the onset of and throughout exercise, its development results in a faster metabolic attainment of the

oxygen demands of an exercise intensity (τ) and may also reduce the progressively greater energy turnover associated with prolonged exercise (slow component (Burnley and Jones, 2007; Jones and Burnley, 2009). Another factor which behaves similarly to the $\dot{V}O_2$ slow component is that of ventilatory threshold.

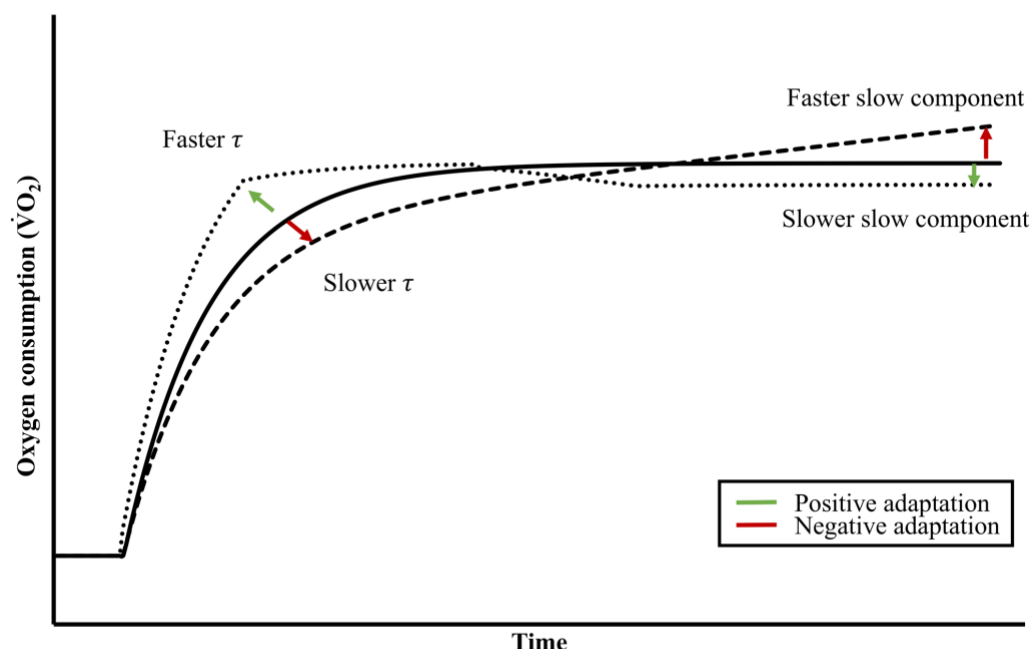


Figure 2-1 A typical $\dot{V}O_2$ kinetics curve, with faster and slower fast and slow components also illustrated

Ventilatory threshold (VT), measured in $L \cdot min^{-1}$, is a common marker used to establish the onset of anaerobic respiration, and has been moderately correlated with 40 km cycling time trial performance (Amann *et al.*, 2004) and the pace sustained for a marathon (Loftin *et al.*, 2007). Ventilatory threshold (VT) can simply be defined by assessing a change in the behaviour of ventilation ($\dot{V}E$); below the VT $\dot{V}E$ displays a linear response to increasing exercise intensity, whereas above VT the behaviour of $\dot{V}E$ is a non-linear exponential (Sigmoid curve). The concept of VT was developed by Wasserman & McIlroy (1964) and documents, through respiratory assessment, a shift in metabolic conditions from aerobic to anaerobic. When VT is passed, arterial concentration of bicarbonate is rapidly lowered and there is an onset of blood lactate accumulation (OBLA; (K. Wasserman and McIlroy, 1964)). Thus, the velocity corresponding to VT can be considered an assessment of the maximal respiratory aerobic steady state, differing to $\dot{V}O_{2max}$ which is an independent but interrelated respiratory marker. Age and training affect ventilatory properties, with younger individuals expected to possess larger $\dot{V}E$ capacity (Blackie *et al.*, 1991; Everman *et al.*, 2018), with a greater $\dot{V}E_{max}$ attained due to

training in one's youth considered protective of aerobic fitness as one ages (Everman *et al.*, 2018).

Athletes are capable of exercising at higher absolute ventilatory values ($\text{L}\cdot\text{min}^{-1}$) than sedentary counterparts (Faull, Cox and Pattinson, 2016), with similar differences seen when adults are compared to children (Mahon, Gay and Stolen, 1998), yet when $\dot{V}\text{E}$ is expressed as a % $\dot{V}\text{O}_{2\text{max}}$ similarities are seen across populations (Mahon, Gay and Stolen, 1998; Fabre *et al.*, 2013; Faull, Cox and Pattinson, 2016; Everman *et al.*, 2018). Importantly, ventilatory responses display differences between exercise modalities (running vs. cycling), most likely due to differences in posture and resultant muscular recruitment (Hue *et al.*, 2000; Tanner, Duke and Stager, 2014). Triathletes provide a unique example of this fact, as they have been reported to produce consistent ventilatory responses in running and cycling tasks within themselves and display similar $\dot{V}\text{O}_{2\text{max}}$ values to single sport specialists, but when compared to runners of matched ability possess a lower VT (Hue *et al.*, 2000), suggesting a sport specific ventilatory signature possibly forged through a comparatively greater training volume at the velocity associated with VT or a relative neglect of running in comparison to cycling when expressed as a percentage of training duration/volume (Hue *et al.*, 2000; Neal, Hunter and Galloway, 2011; Mujika, 2014).

In conclusion, $\dot{V}\text{O}_2$ kinetics and VT may limit endurance performance, both are respiratory parameters that display development following endurance training; such development is also likely to affect substrate utilisation during exercise which is discussed presently.

2.2.1.4 Substrate use

The fuel preferentially selected for metabolism during exercise is largely dependent upon exercise duration and exercise intensity, but may also be influenced by acute nutrition, biological sex, body composition, (genetic or lifestyle) disease state, habitual diet and training status. To simplify the forthcoming discussion, protein is sparingly oxidised during exercise and typically only constitutes 2-3% of the energetic contribution to exercise, this may increase during prolonged or fasted exercise (Gibala, 2007), but is still limited due to the importance of nitrogen containing processes within the body (Weber, 2011), hence a desire to minimise the oxidation of branched chain amino acids (Gibala, 2007) and spare protein during aerobic exercise. For this reason, respiratory gas analysis typically assumes protein to have a fixed contribution during exercise and is not commonly reported; this contribution will vary depending on the analysis method used.

The energetic contribution from carbohydrate (CHO) increases with exercise intensity, and decreases as exercise duration becomes prolonged. Fat oxidation though displays an inverse relationship with exercise intensity and increases in energetic contribution as exercise duration increases. These changes in substrate use are expressed either by the respiratory exchange ratio (RER) or the respiratory quotient (RQ); RER is calculated by dividing $\dot{V}CO_2$ by $\dot{V}O_2$ and is commonly used as a measure of exercise intensity and a secondary marker of volitional exhaustion during maximal exercise (Deuster and Heled, 2008). This value can exceed 1.0 under non-steady state exercise conditions and therefore reflects the increased ventilatory rate and lactate [La] metabolism brought about by increased CO_2 production (Goedecke *et al.*, 2000). Whereas RQ is used to determine the substrate being oxidised at rest or during steady state conditions and cannot exceed 1.0 as it is reflective of the substrate being oxidised at the level of the tissue (Deuster and Heled, 2008). In both instances values <0.8 are thought to reflect exclusively fat oxidation, 0.8-0.9 are representative of mixed metabolism (CHO and fat oxidation) and values ≥ 1.0 indicate exclusively carbohydrate oxidation (Romijn *et al.*, 1993; G. A. Brooks and Mercier, 1994; Deuster and Heled, 2008; Dasilva *et al.*, 2011). Ketosis may induce lower RER/RQ values of 0.66-0.73, having been induced either by exercise, a ketogenic diet, consumption of exogenous ketone esters or salts or prolonged fasting (Evans, Cogan and Egan, 2016). Ketogenic diets may be used in the treatment of some clinical conditions (e.g. Epilepsy and McArdle's disease (Vorgerd and Zange, 2007; Boison, 2017)) as ketones provide a viable alternative substrate for the brain, but the balance of the evidence does not support their adoption in competitive endurance performance (Burke, 2015; Evans, Cogan and Egan, 2016; Burke *et al.*, 2017; Burke and Hawley, 2018).

Endogenous sources of CHO present an efficient but limited source of rapidly oxidised fuel for the body. One gram (1g) of CHO contains ~4kcal and when oxidised can produce 5.05kcal of energy, but stores are limited to an approximate maximum of 3000kcal in a 70kg trained male, across plasma (20kcal), hepatic (650kcal) and muscle (2300kcal) sources (Rapoport, 2010). Conversely fat presents a relatively unlimited source of fuel in even the leanest individuals, but is inefficiently and slowly oxidised, as 1g of fat (9kcal) yields only 4kcal of work and therefore requires more oxygen to be consumed for complete oxidation (Rapoport, 2010).

The constraints of endogenous substrate use are overcome by the ingestions of exogenous fuel sources. Research has centred on CHO provision, with increases in the rate of carbohydrate consumption and the ingestion of a combination of carbohydrate sources recommended as exercise duration increases (Jeukendrup, 2014; 2017). Training one's

stomach to tolerate these strategies is also encouraged (Jeukendrup, 2014; de Oliveira, Burini and Jeukendrup, 2014; Costa, Hoffman and Stellingwerff, 2018), and is likely limited by the number of glucose transporter proteins dedicated to each monosaccharide (SGLT-1 and GLUT5; glucose and fructose, respectively) within the intestinal lumen (Jeukendrup, 2014; 2017). The use of alginate has recently been thought to increase the upper tolerable limit of carbohydrate ingestion during exercise (Sutehall *et al.*, 2018), evidence is preliminary despite alleged widespread use by elite athletes in major marathons.

Another strategy that has been shown to increase the availability of CHO during exercise is carbohydrate loading. Carbohydrate loading consists of increasing one's CHO intake in the days preceding an event, increasing hepatic and muscle glycogen stores through super-compensation (Rapoport, 2010; D. T. Thomas, Erdman and Burke, 2016), typically by 30-100% (Sedlock, 2008), however the degree of glycogen super-compensation does not accurately predict subsequent exercise performance (Sedlock, 2008). Practically, this may mean that an athlete is encouraged to eat ~10-12g.kg⁻¹ of CHO per day, 36 – 48 hours prior to the event (D. T. Thomas, Erdman and Burke, 2016). As with the provision of exogenous CHO during exercise, an athlete may be encouraged to consume sources of multiple transportable CHO e.g. fruit juice (fructose), confectionary (glucose), rice or pasta (starchier complex carbohydrates).

On the other hand, exogenous fat intake during exercise, either through ingestion of medium chain triglycerides or long chain triglycerides is discouraged. Neither strategy enhances performance, and is associated with increased prevalence of gastrointestinal upset (Hawley, 2002). Glycogen sparing i.e. a reduction in glycogenolysis and or CHO oxidation (15 – 48% reduction; Hawley, 2002), is seen during moderate to high intensity aerobic exercise (65-90% $\dot{V}O_{2max}$) following increases in fat availability during exercise. However, chronic feeding of a high fat diet doesn't necessarily impair one's ability to resynthesize glycogen (Volek *et al.*, 2016) but does impair one's ability to oxidise CHO in as little as five days (Stellingwerff, 2005), most likely through downregulation of PDH and upregulation of hormone sensitive lipase (Stellingwerff, 2005), in essence these adaptations are 'glycogen impairing' as opposed to 'glycogen sparing' (Burke, 2015).

To conclude, the evidence presented suggest that maximising CHO oxidation and provision during exercise leads to either a faster and or more economical performance due to an increased metabolic return of CHO per g, and lower $\dot{V}O_2$ consumption. This can be further increased through feeding of exogenous CHO during exercise, or by carbohydrate loading. Alginates represent an emerging but heavily commercialised future research

direction, whereas the provision of fat during exercise would inhibit CHO oxidation, and may increase the risk of gastrointestinal distress. Ultra-endurance exercise is limited in a different way, nutritionally speaking, to classical endurance distances due to the prolonged nature and logistical challenges of such events, for further information the reader is directed to recent reviews on nutrition (Costa, Hoffman and Stellingwerff, 2018) and hydration (Hoffman, Stellingwerff and Costa, 2018) for ultra-endurance events.

2.2.2 Psychological

Whilst there is a body of literature that assesses the psychological nature and sources of fatigue; for the purpose of this thesis these factors and models are considered to be manifestations and subsequent interpretation and interaction of underlying chemical, physiological and nutritional statuses that potentially alter central and peripheral factors, at or below the level of the brain. Such factors are elaborated upon in subsequent sections, and so this section serves to briefly introduce key concepts and direct the reader to thorough reviews of literature in these areas. For a review of the potential role of neurotransmitters in fatigue please see (Roelands *et al.*, 2013; Roelands, De Pauw and R. Meeusen, 2015), with a review of psychological determinants of endurance exercise performance provided by McCormick (McCormick, Meijen and Marcora, 2015).

2.2.3 Environmental

This section will briefly describe environmental factors that may impair endurance exercise performance, with comment upon the physiological mechanisms by which they limit performance, and how they have been attenuated to date. Acclimation and acclimatisation strategies will not be discussed at length, but are included to provide an impression as to the time course of physiological adaptations and performance recovery under each environmental condition.

2.2.3.1 Altitude

Increases in altitude, decrease the partial pressure of oxygen and therefore reduce the rate at which oxygen can saturate red blood cells as they move through capillaries around alveoli. This lower partial pressure, coupled with the increased aerobic demand of (endurance) exercise places significant strain upon an athlete and limits exercise through a reduction in oxygen availability and uptake at the muscle and subsequent downstream metabolic effects. These may include, but are not limited to, an increase in carbohydrate metabolism (P. U. Saunders, Pyne and Gore, 2009; West, 2012), suppressed appetite

(Wasse *et al.*, 2012), decreased $\dot{V}O_{2\max}$ (and therefore an increased % $\dot{V}O_{2\max}$ for a fixed intensity), increased rating of perceived exertion for the same exercise intensity (Sharma *et al.*, 2017), and endurance performance reductions of 10-20% slower than sea level records (P. U. Saunders, Pyne and Gore, 2009)

The body undergoes a range of cardiovascular, haematological, hormonal and metabolic adaptations in response to altitude exposure, with most driven by hypoxia inducible factor 1 alpha (HIF-1 α) which acts as a signalling molecule for a range of transcription processes (West, 2012). With respect to the cardiovascular system, acute altitude exposure causes an increase in heart rate, stroke volume, and consequently cardiac output (Samuels, 2004; West, 2012; Brown and Grocott, 2013; Khodaei *et al.*, 2016). Erythropoiesis (increased red blood cell production) increases the haemoglobin content of the blood by increasing the number of red blood cells due to erythropoietin (EPO) secretion (Baker and Parise, 2016; Płoszczyca, Langfort and Czuba, 2018), and supports this by reducing plasma volume content (Płoszczyca, Langfort and Czuba, 2018) to increase the relative oxygen carrying capacity of the blood via haemoconcentration. This is the primary adaptation that is of interest to endurance athletes, and is illegally accelerated in athletes either through the use of recombinant EPO (Sgrò *et al.*, 2018), or by blood doping (Fitch, 2017). There is also an increased anaerobic and therefore CHO contribution during exercise when at altitude, meaning a greater blood lactate response for lower intensity exercise than at sea level; this has performance and training implications, as repetition duration or intensity may need to be reduced, or recovery interval duration increased. In mountaineers these changes can occur rapidly, notably altering within 15 days despite ascending in altitude up to >4000m during this time (Windsor and Rodway, 2007). The time course of adaptation to altitude is like that of heat, which is outlined in section 2.2.3.3. Athletes may also benefit from undertaking extended training stints at altitude with durations of 21-28 days at 2000-3000m reported (J. Daniels and Oldridge, 1970; Chapman *et al.*, 2016; Sharma *et al.*, 2017), however lower altitudes (1600-1800m) may also be effective in improving performance through adaptations mediated by other factors as opposed to haematological adaptations to altitude (Sharma *et al.*, 2019). The author's experience supports this, having spent 35 days at 1500-2300m, and demonstrating improvements in body composition and 5km performance (unpublished observations).

It is worth noting that whilst altitude clearly limits performance, and the use of altitude to improve performance may be contested in elite athletes (G. P. Millet *et al.*, 2016; Lundby and Robach, 2016) if a sufficiently potent and thoughtfully monitored altitude stimulus is applied to a supreme athlete, incredible performances are possible, as detailed in Millet's

case study of Kilian Jornet, who produced the fastest rate of vertical climbing up to 8000m (350m/h; 6400m to 8000m) and scaled Mt. Everest twice within one week (G. P. Millet and Jornet, 2019).

2.2.3.2 Cold

Exposure to cold induces physiological, morphological and behavioural changes in an individual (Makinen, 2010); these changes depend on the length of cold exposure, the nature (air or water; single or repeated) and the severity of the cold stimulus being applied, if improperly managed these factors may produce cold injuries (Steine *et al.*, 2003; Guly, 2012). From an endurance perspective, cold presents a homeostatic challenge as the rate of heat loss may exceed heat storage during exercise in a sufficiently cold environment, presenting an energetically expensive conflict to the athlete, who must maintain a sufficient T_{core} whilst expending energy to perform. Upon initial cold exposure, one can expect a hypothermic response. Typically, this will involve a reduction in temperature at the core and periphery driven by vasoconstriction and a reduction in metabolic heat production (Tipton *et al.*, 2013; Brazaitis *et al.*, 2014; Daanen and van Marken Lichtenbelt, 2016; O. R. Gibson *et al.*, 2017; J.-Y. Lee, Park and Kim, 2017; K. Gordon *et al.*, 2019), which may be countered by an increase in shivering thermogenesis (Makinen, 2010), with non-shivering thermogenesis and rates of lipolysis (K. Gordon *et al.*, 2019) elevated and respiratory exchange ratio reduced (Muller *et al.*, 2012) following chronic cold exposure(s).

Shivering and thermal sensation may show signs of habituation following the first exposure to the cold (Budd, 1989; Makinen, 2010; Brazaitis *et al.*, 2014; Daanen and van Marken Lichtenbelt, 2016), and may display localised adaptation that facilitate performance of musculature in the cold (J.-Y. Lee, Park and Kim, 2017). Subjective adaptations may alter behavioural thermoregulation strategies. This presents a double-edged sword of sorts: for athletes competing at high metabolic intensities an improvement in thermal sensation and reduction behavioural thermoregulation may improve performance through permitting a greater rate of metabolic heat production during exercise whilst concomitantly limiting distractions related to cold sensation, whereas for an athlete that is exposed to either extreme cold and or must perform in a cold environment for an extended period e.g. a Polar explorer, such an adaptation may pose an increased risk of cold injury.

The above evidence suggests that for endurance athletes, cold may be best combatted behaviourally, by wearing additional clothing such as hats, gloves and arm warmers,

hereby reducing the need for targeted acclimation strategies but highlighting the importance of combatting cold so as to mitigate its effects upon performance.

2.2.3.3 Heat

Heat as a driver of fatigue, and the resultant physiological, metabolic and perceptual effects are discussed in Section 2.4. Simply, heat poses a multi-systems threat to the body during endurance exercise; these effects are exacerbated by increasing exercise duration or intensity but can be mitigated by targeted physiological or perceptual cooling strategies. Longer term adaptations that better equip an athlete to tolerate exercise performance in the heat are known as heat acclimation or acclimatisation strategies. Acclimation takes place in artificial indoor environments, whereas acclimatisation takes place *in situ* under hot natural conditions (Racinais *et al.*, 2015).

Acclimation strategies typically consist of repeated exposure to an artificial hot environment with recommended daily session durations of 30-60 min, for a period of two weeks (Racinais *et al.*, 2015). This duration of acclimation will result in adaptations in a full complement of physiological and subjective variables (Périard, Racinais and Sawka, 2015), these are discussed in subsequent sections (2.4 and associated subsections), but is important to note that these variables display differing time courses of adaptation, typically ranging from seven to fourteen days (Périard, Racinais and Sawka, 2015), commencing on the first day of heat exposure and demonstrating 75 – 80% of change within the first 7 days (Shapiro, Moran and Y. Epstein, 1998; Pandolf, 1998).

A recent paper (Willmott *et al.*, 2016), investigated two short term heat acclimation protocols (four days; 35°C and 60% relative humidity) and assessed the differences in performance resulting from either twice daily or daily heat exposure upon 3km time trial performance (2km at 40% $\dot{V}O_{2max}$ + 3km maximal effort). Neither group differed statistically when compared to control ($p = 0.35$; -6 ± 44 s or $+0.6\%$), yet the differences were on average practically meaningful (twice daily: -36 ± 34 s or $+3.5\%$; once daily: -26 ± 28 s or $+2.8\%$), but displayed wide standard deviations suggesting a variable response to either heat stress or training and possibly recovery from the initial performance test. This latter point is pertinent not only due to the short-term nature of the intervention, but the athletes in each group displayed only moderate maximal oxygen uptake values as categorised by De Pauw & Roelands (45.0 – 54.9 ml.kg⁻¹.min⁻¹ i.e. Performance Level 2; (De Pauw and Roelands, 2013)), effectively priming them for adaptation to the additional stimulus provided by heat.

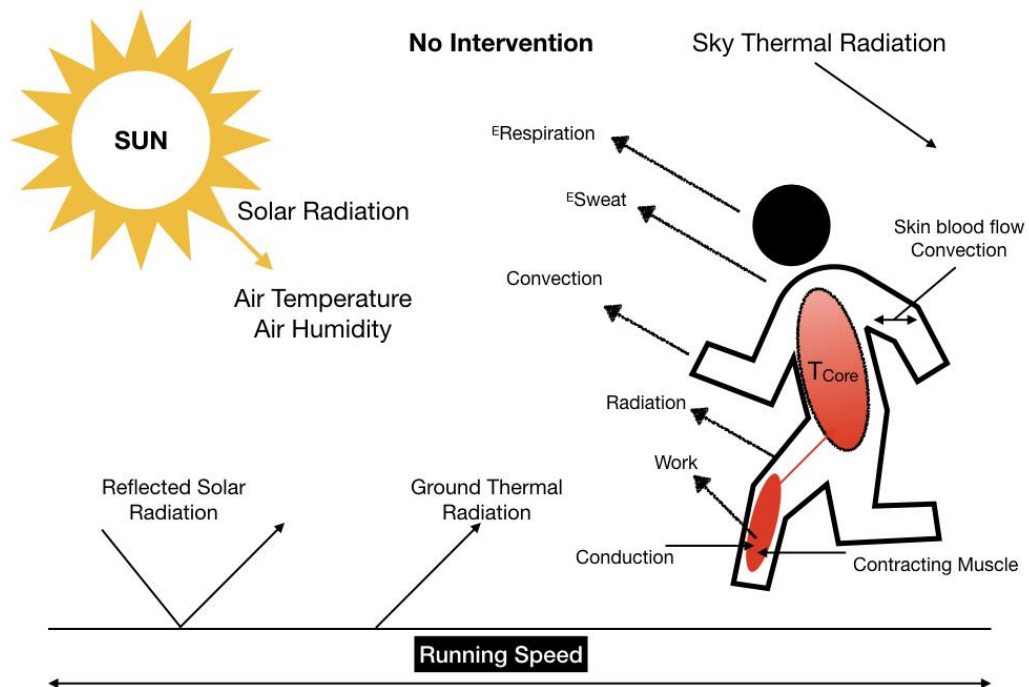
The use of additional clothing during exercise may also present a short - moderate term heat acclimation option as it increases core temperature and sweat rate which are considered primary drivers of heat adaptation (Stevens, 2018; Willmott *et al.*, 2018). Additional clothing would also reduce evaporative cooling and create a localised heat storage response; this is of greater concern to cyclists than runners due to faster training velocities, resultant wind speed and therefore potential rate of evaporative cooling (Shimazaki, Yoshida and Yamamoto, 2015). Post-exercise hot water immersion (Zurawlew *et al.*, 2016; Zurawlew, Mee and Walsh, 2018) at 40°C for ≤ 40 min after moderate intensity exercise has also been shown to induce thermoregulatory adaptations after as little as six days exposure. Immersion in hot water extends the time at an elevated core temperature following exercise, effectively lengthening and intensifying the thermal load placed upon an athlete following a session. It is unclear whether complete immersion is necessary to drive these adaptive processes, or if a partial immersion of the exercising musculature (e.g. legs only) would be sufficient to induce a localised response that is still ergogenic.

2.2.3.4 Humidity

Humidity is often paired with heat in exercise trials to produce a thermally challenging and uncomfortable environment, acts independently of (Maughan, Otani and Watson, 2012; Junge *et al.*, 2016) and concomitantly with temperature to produce thermoregulatory responses in athletes (Maughan, 2010). Humidity is a measure of the amount of moisture within the air (%) and thus affects and is reflective of the evaporative capacity of an athlete, potentially limiting the rate at which an athlete can dissipate heat through evaporative sweat losses (Gagnon, Jay and Kenny, 2013; Kenny and Jay, 2013; C. J. Smith and J. M. Johnson, 2016). Humidity is limiting as an increase in humidity directly decreases the moisture concentration gradient between the skin and the environment (Maughan, 2010). If these two factors reach a point of equilibrium, sweat is retained upon the skin and local skin temperature (T_{skin}) increases rapidly, concomitantly increasing blood temperature, whilst lessening the body's ability to cool itself, as an increase in blood temperature would manifest as an elevated T_{core} . This decrease in concentration gradient between the core and the periphery may lead to fatigue in most instances, and can be a driver for heat related illness (American College of Sports Medicine *et al.*, 2007).

2.2.3.5 Radiant heat

Radiant heat, or solar radiation, is an often-neglected part of study protocols, but in ecologically valid settings is a contributory factor to a decline in endurance performance (R. R. Gonzalez *et al.*, 2012; Otani *et al.*, 2016; 2017; 2019), as the sun can contribute approximately 500W of further thermal load to an athlete's already stressed system (Nielsen, Kassow and Aschengreen, 1988; Otani *et al.*, 2016; 2017). Factors that may influence the radiant heat load placed upon an athlete include the time of day (Otani *et al.*, 2017) and associated angle of the sun (R. R. Gonzalez *et al.*, 2012), clothing worn by participants and the activity being performed in them (Nielsen, 1990; Wheeler, 1991; M. R. Ely, Chevront and Montain, 2007; R. R. Gonzalez *et al.*, 2012; Otani *et al.*, 2016; 2017; 2019). Depending upon the exercising surface, this could also be reflected or transmitted by the ground (Figure 2.1), incurring a further cost and potentially worsening endurance exercise performance.



Adapted from Gisolfi & Wenger, 1984

Figure 2-2 Schematic diagram showing sources of human heat production, transfer and loss

Table 2-1 IAAF Championship, Diamond League & World Challenge Fixtures with accompanying average temperatures for time of year

Date	Meeting	Venue	Country	Average Temperature (°c)
21 March 2015	IAAF Melbourne Wold Challenge	Melbourne	Australia	19
02 May 2015	IAAF World Relay Championships	Nassau	Bahamas	26
09 May 2015	Jamaica International Invitational	Kingston	Jamaica	28
10 May 2015	Seiko Golden Grand Prix	Kawasaki	Japan	22
15 May 2015	IAAF Diamond League	Doha	Qatar	39
17 May 2015	IAAF Diamond League	Shanghai	China	25
20 May 2015	2015 IAAF World Challenge Beijing	Beijing	China	27
23 May 2015	IAAF World Challenge Dakar	Dakar	Senegal	26
24 May 2015	AA Drink FBK-Games	Hengelo	Netherlands	19
26 May 2015	54 th Ostrava Golden Spike	Ostrava	Czech Republic	20
29 – 30 May 2015	Prefontaine Classic	Eugene	United States of America	19
04 June 2015	Golden Gala Pietro Mennea	Rome	Italy	29
07 June 2015	Sainsbury's Birmingham Grand Prix	Birmingham	United Kingdom	19
11 June 2015	ExxonMobil Bislett Games	Oslo	Norway	20
13 June 2015	IAAF Diamond League	New York	United States	27
14 June 2015	Mohammed VI d'Athletisme	Rabat	Morocco	25

04 July 2015	Meeting Areva	Paris	France	25
09 July 2015	Athletissima	Lausanne	Switzerland	25
11 July 2015	33 rd Meeting Madrid 2015	Madrid	Spain	33
17 July 2015	Herculis	Monaco	Monaco	27
24 – 25 July 2015	Sainsbury's Anniversary Games	London	United Kingdom	23
30 July 2015	Stockholm BAUHAUS Athletics	Stockholm	Sweden	22
22 – 30 August 2015	IAAF World Championships	Beijing	China	31
03 September 2015	Weltklasse Zurich	Zurich	Switzerland	20
06 September 2015	ISTAF Berlin	Berlin	Germany	19
08 September 2015	IAAF World Challenge Zagreb	Zagreb	Croatia	21
11 September 2015	Memorial van Damme	Brussels	Belgium	19
13 September 2015	Rieti Meeting 2015	Rieti	Italy	25
13 September 2015	Grande Premio Brasil Caixa Sao Paulo de Atletismo	Sao Paulo	Brazil	25

2.3 Models of fatigue; with particular reference to endurance performance

Seminal writings at the genesis of physiological investigation and reflection sought to better understand and categorise fatigue. Brillat-Savarin in 1825 proposed three kinds of fatigue, notwithstanding hunger, namely muscular fatigue, mental labours and amorous excesses (Brillat-Savarin, 2009). The Italian physiologist Angelo Mosso, who has been credited as the first to purposefully investigate fatigue (Meeusen *et al.*, 2006; Enoka and Duchateau, 2008; Marino, Gard and Drinkwater, 2009; Maughan, 2010; McMorris, Barwood and Corbett, 2018), writes later ‘The first is a diminution of the muscular force. The second is fatigue as a sensation. That is to say, we have a physical fact which can be measured and compared, and a psychic fact which eludes measurement.’ (Mosso, 2017). Both Brillat-Savarin and Mosso acknowledge the potential for physiological and psychological sources of fatigue, and their coming together to affect the individual by a reduction in or cessation of the action(s) which have led to the fatigued state. Exercise and associated scientists have since sought to further identify and investigate mechanisms responsible for fatigue, and provide an explanatory model of fatigue. Typically, models are confined to a single professional lens, possibly due to confirmation or conservatism biases, or salience (Robergs, 2017). These can be divided simply into models that exist ‘above the neck’ i.e. central and psychological models and ‘below the neck’ i.e. at the level of muscle, organs and the periphery. There are also integrated models, that encompass psychological and physiological determinants. The discussion of these models will focus on work conducted in or relevant to endurance sports.

2.3.1 Above the neck

Fatigue may be considered to occur ‘above the neck’ if there is neurological input or interpretation that results in the cessation of exercise. This does not always occur at a conscious level and may be enhanced with training or impaired with prior cognitive work (Marcora, Staiano and Manning, 2009). Biologically, above the neck fatigue is central in nature and involves the brain, brain stem and spinal column but does not project into circulation or working musculature. Psychological explanations of (central) fatigue are also mentioned.

2.3.1.1 *The Central Governor*

The Central Governor theory was first proposed by Timothy Noakes’ laboratory in the early 2000’s as part of a series of papers (Gibson and Noakes, 2004; Noakes and Gibson, 2004; Noakes, Gibson and Lambert, 2005; Lambert, Gibson and Noakes, 2005). These

papers argue that traditional models of fatigue emphasise fatigue as a peripheral phenomenon (Gibson and Noakes, 2004) that is an example of a linear progression until a point of catastrophic failure, deemed the cardiovascular, anaerobic, catastrophe model in some works (Noakes and Gibson, 2004; Weir, 2006). This critique of a peripheral approach to fatigue is extended by suggesting that peripheral approaches are reductionist, teleological and are essentially a product of a researcher's professional lens e.g. a physiologist may attribute fatigue to a discrete variable such as diminished ATP, or increased blood lactate concentrations because that is what they are trained to measure (Lambert, Gibson and Noakes, 2005).

In contrast, Noakes and colleagues suggest that through a form of 'black box thinking' in which neural signals from the periphery are integrated and fed back to the brain and fed forward to the muscles in an oscillatory fashion (Gibson and Noakes, 2004; Lambert, Gibson and Noakes, 2005), suggesting that fatigue is therefore a sensory factor as opposed to being attributable solely to peripheral factors. The Central Governor is theorised to mediate these competing signals in a non-linear and deterministic fashion which ultimately expresses as fatigue, unlike a peripheral model, whereby fatigue is defined by a linear or exponential accumulation or diminution of a metabolite, and so is a correlate as opposed to a cause or conclusion of exercise performance.

More recently the Central Governor extended its reaches to a much wider range of variables, effectively suggesting that any variable can influence exercise performance and thus fatigue (Noakes, 2012; Inzlicht and Marcora, 2016). Athletic performance per the Central Governor model is a (sub)conscious expression of how an athlete copes with and interprets a plethora of factors, informed and managed via feedforward and feedback mechanisms, as such fatigue is illusory, and a subconscious decision with respect to exercise performance (Noakes, 2012). This notion has been previously challenged by Weir (2006) who rightly points out that despite suggesting fatigue is an emotion or sensation, in studies designed to assess the Central Governor the same variables are assessed as in other exercise trials and so may be flawed in their design and interpretation. A more pressing issue is that raised by Inzlicht & Marcora (2016) that under its current guise the Central Governor is not falsifiable. Originally Noakes and colleagues (Noakes, Gibson and Lambert, 2005) suggested that the governor regulated at a subconscious level and couldn't be overridden due to the impending threat upon homeostasis. In light of recent evidence to suggest that exercise performance can indeed be overridden consciously (McCormick, Meijen and Marcora, 2015), the model was simply updated (Inzlicht and Marcora, 2016) and so became unfalsifiable. To conclude, the Central Governor presents an intuitive and

attractive explanation for fatigue, but as a model it is deeply flawed due to its inability to be falsified, variables of choice at the point of assessment and general approach as a theoretical panacea in the absence of accompanying biology. An advance on the Central Governor may be an interoceptive approach to fatigue, which employs known regions of the brain to proffer an explanation – this is outlined in section 2.3.3.2, having first explored other above and below the neck models of fatigue.

2.3.1.2 Motivational Intensity and the Psychobiological Model of fatigue

Motivational Intensity theory (Brehm and Self, 1989) is regarded as the predecessor to the psychobiological model of exercise tolerance (Marcora, 2008; 2009); Brehm and Self (1989) characterise motivational intensity as the effort one is willing to expend in pursuit of a motive, and the time over which this effort is distributed. The psychobiological model of fatigue builds upon this by suggesting that fatigue attributed to maximal exercise is the result of task disengagement i.e. the participant is no longer sufficiently motivated to complete the task, and time to exhaustion or performance is the result of how an athlete's motivation has been distributed over task duration (Marcora, 2008; 2009; Marcora and Staiano, 2010).

Marcora's argument for this is often that maximal ratings of perceived exertion are recorded upon task completion, and this value scales with task duration (Marcora and Staiano, 2010). These findings are somewhat supported by the fact that mental fatigue can increase the rate at which RPE accumulates throughout a task, but no differences are reported at exhaustion (Marcora, Staiano and Manning, 2009), with no differences in success ($p < 0.524$) and intrinsic ($p < 0.126$) motivation between groups observed neither pre nor post-trial. This is counterintuitive as reductions in motivation would at least be expected at the pre-trial measurement, if mental fatigue indeed impaired exercise performance via the mechanism proposed by the psychobiological model.

The authors do note though that this may have been a self-inflicted null finding, due to the offering of a monetary reward for the best cycling performance (Boksem, Meijman and Lorist, 2006; Marcora, Staiano and Manning, 2009); thus the limitation should also be taken into account in their subsequent work (Marcora and Staiano, 2010) which employed a systematic approach to falsifying their hypothesis by assessing maximal power output at 25% intervals of a previously established TTE, and noted a reduction in maximal power output as percentage of TTE increased despite required power output remaining unchanged. Motivation was not measured in this experiment so the reduction in maximal power output cannot be attributed to a reduction in motivation in this instance.

Motivation has however been shown to interact with other self-report psychological measures and influence ultra-endurance running performance (Best, Barwick, *et al.*, 2018) and may also present as a possible explanation for the ‘end-spurt phenomenon’ often seen in the latter stages of endurance events (Pageaux, 2014; K. Thomas *et al.*, 2015), especially in instances of head to head competition (Corbett *et al.*, 2012) although this explanation may require further qualitative support by athletes for confirmation.

Despite documented disagreements within the literature (Noakes and Tucker, 2008; Marcora, 2008; Inzlicht and Marcora, 2016), the psychobiological model and the central governor are similar in nature. Both place importance upon subconscious sensory information and its role within the generation of a conscious rating of perceived exertion, and subsequent conscious interpretation (Marcora, 2008; Noakes and Tucker, 2008). Where the models differ is the time point at which their explanation for fatigue is most valid and how they apportion ‘blame’ upon the athlete.

The central governor model proposes that exercise performance is regulated in a feedforward mechanism and so explains exercise end-point, from the onset of exercise. Whereas the psychobiological model considers fatigue a mismatch between motivational intensity and task demand and as such emphasises exercise end-point immediately prior to exercise termination. Whilst these are important theoretical differences, evidence that exercise end-point can be extended through strategies such as deception, experimenter sex, external reward and verbal encouragement (Richter and Gendolla, 2009; Lamarche, Gammage and Gabriel, 2011; Castle *et al.*, 2012; McCormick, Meijen and Marcora, 2015; D. N. Borg *et al.*, 2018) suggest that the psychobiological model of fatigue proffers the better explanation of exercise termination. Noakes (2012) argues that athletes who lose races may do so as the result of a predetermined conscious decision, and fatigue is simply the symptom of this. However, evidence from head to head competitive studies positively counters this assertion (Corbett *et al.*, 2012; 2017) as the presence of a competitor yields higher power outputs attributed to an increased anaerobic contribution (Corbett *et al.*, 2012) and impaired thermoregulatory behaviours (Corbett *et al.*, 2017), possibly to athletes’ detriment. It is unlikely that such behaviours are premeditated, but are driven by an increase in motivation, accompanied by a knowledge of exercise end-point (Pageaux, 2014). This is supported fourfold: firstly, by non-significant differences in other perceptual thermal measures between solo and head to head performances; secondly, the athletes accrued the most heat demonstrated the greatest improvement in time between head to head and self-paced conditions (Corbett *et al.*, 2017). Thirdly, athletes performing in head to head conditions may negate an end-spurt but still perform faster overall due to sustaining

a higher exercise intensity throughout the effort (Corbett *et al.*, 2012; Renfree and A. S. C. Gibson, 2013) and finally, central governor proponents present a version of the psychobiological model under the guise of ‘affective load’ and acknowledge the importance of motivation and its optimisation in relation to task completion and duration in a 2011 review (Baron *et al.*, 2011).

2.3.2 Below the neck

Theories of fatigue that are considered ‘Below the neck’ attribute fatigue to systems that occur at the periphery. These systems are predominantly involved in the transport of energetic substrates or the conservation thereof, function at the level of the muscle contractile unit or thermoregulation. It is acknowledged that signals are fed-forward or fed-back to these systems from associated brain areas, however fatigue in these systems typically corresponds to a threshold or they may contain a local protective safety mechanism that can be attenuated or exacerbated, and as such are capable of fatiguing independent of brain input.

2.3.2.1 AV Hill and $\dot{V}O_{2max}$, exercise economy and the lactate threshold

The following section provides an overview of the cardiorespiratory limits to endurance exercise performance, commencing with the classic work of Nobel Laureate A.V. Hill, who first defined steady state exercise and maximal oxygen consumption ($\dot{V}O_{2max}$) and in doing so identified a linear relationship between oxygen consumption ($\dot{V}O_2$) and running speed (A. V. Hill and Lupton, 1923). To clarify, $\dot{V}O_{2max}$ is the maximum volume of oxygen that one can take up and use to perform muscular work; this value does not increase despite an increase in oxygen demand, and is limited by cardiovascular and respiratory factors (Bassett and Howley, 1997; 2000), so a plateau in $\dot{V}O_2$ may be seen; secondary measures such as an RER > 1.1 or an RPE of ≥ 18 (Abbiss *et al.*, 2015) confirm attainment of $\dot{V}O_{2max}$. Maximal oxygen consumption can be expressed in absolute ($L \cdot min^{-1}$), or relative terms ($ml \cdot kg \cdot min^{-1}$), and whilst certainly trainable, one’s genetics may influence $\dot{V}O_{2max}$ baseline values and the trainability of one’s $\dot{V}O_{2max}$ (Williams *et al.*, 2017).

The concept of a $\dot{V}O_2$ plateau was also proposed by Hill, if exercise intensity (oxygen requirement) progresses beyond the rate of oxygen consumption then one incurs an oxygen debt, however oxygen consumption plateaus as the circulatory and respiratory systems are performing maximally. The presence of a plateau is a point of contention within the literature (Noakes, 1998; 2008), but may not occur in some individuals due to an inability to sustain the intensity long enough for a plateau to occur (Hawkins *et al.*, 2007) or that

the exercise intensity is such that $\dot{V}O_2$ is still climbing at the point of volitional exhaustion (D. W. Hill, Poole and J. Smith, 2002), and may also be attributed to data sampling and processing differences (e.g. breath by breath vs. 30 sec sampling (Myers *et al.*, 1990; Bassett and Howley, 1997).

Mechanistically, $\dot{V}O_{2\max}$ is the result of one or more cardiorespiratory variables reaching a point of limitation:

The first possible limitation is at the point of delivery of oxygen to the red blood cell; arterial saturation of oxygen (SaO_2) may be reduced at high work rates. Decreased SaO_2 may be caused by the high rate at which blood is shuttled through arterial capillaries, resulting in a lower percentage saturation; this is especially true in elite athletes, who possess a much higher cardiac output (\dot{Q}) than untrained individuals ($40L\cdot min^{-1}$ v $25L\cdot min^{-1}$) and so this greater volume, moving at a higher velocity decreases the likelihood of SaO_2 prior to exiting pulmonary capillaries. This limitation is also apparent at altitude, where the partial pressure of oxygen is lower and so the forcing effect typically caused by increased alveolar-arterial difference of O_2 is reduced, at the point of the alveoli. This results in a decreased SaO_2 at altitude, and thus a decreased capacity for exercise and $\dot{V}O_{2\max}$ at altitude (J. Daniels and Oldridge, 1970; P. U. Saunders, Pyne and Gore, 2009; Brown and Grocott, 2013; Khodaei *et al.*, 2016), and may serve as a predictor of acute mountain sickness (Castellani *et al.*, 2010; Karinen *et al.*, 2010).

Prior to considering \dot{Q} and its constituent parts, heart rate (HR) and stroke volume (SV), the possible limitations at the red blood cell (RBC) are worth noting. Oxygen saturation may be limited at the point of the RBC by either the number of RBC, or RBC quality i.e. their binding capacity. Both factors limit the haemoglobin (Hb) capacity of the blood, Hb being the protein to which O_2 binds on the RBC. The number of RBC may be increased naturally, through endurance training (Montero *et al.*, 2015) or exposure to altitude (Khodaei *et al.*, 2016; Płoszczyca, Langfort and Czuba, 2018), or artificially through blood doping practices (Brien and Simon, 1987), or the use of recombinant human erythropoietin (Caillaud *et al.*, 2015; Nordsborg *et al.*, 2015; Sgrò *et al.*, 2018), both of which are banned in sport. Haemoglobin concentration may be limited by dietary, exercise associated or sickle anaemias, and by exposure to carbon monoxide and smoking (Malenica *et al.*, 2017); carbon monoxide has a binding affinity to Hb 300 times that of O_2 and exposure leads to the formation of carboxyhaemoglobin, which renders the Hb molecule unable to carry O_2 (Douglas, J. S. Haldane and J. B. Haldane, 1912).

A linear relationship between $\dot{V}O_{2\max}$ and \dot{Q} was first observed by Lindhard in 1915, and supported by Hill and Lupton soon after in 1923 (Bassett and Howley, 2000). This is also

apparent in athletic animals, when compared to their non-athletic counterparts demonstrate a doubling of \dot{Q} and $\dot{V}O_{2\max}$, despite comparable HR_{\max} values (Poole and Erickson, 2011). Further support from SV as the primary factor of \dot{Q} that limits $\dot{V}O_{2\max}$ comes from studies of beta blockers which reduce HR_{\max} and demonstrate a proportional decrease in \dot{Q} and $\dot{V}O_{2\max}$ and a preservation of SV.

Further points of limitation to $\dot{V}O_{2\max}$ occur within the muscle and so are discussed in section 2.3.2.2 *Muscle structure and function*.

As suggested above, $\dot{V}O_{2\max}$ is considered a determinant of exercise performance between fitness groups e.g. recreational to elite, but is not a strong predictor of performance within fitness groups e.g. elite to elite (J. Daniels and N. Daniels, 1992). Within fitness groups, exercise economy i.e. percentage of $\dot{V}O_{2\max}$ required to sustain a given running speed, or $\dot{V}O_2$ to complete a known distance ($\text{ml.kg}^{-1}.\text{km}^{-1}$) are considered better determinants. Absolute speeds coupled with $\dot{V}O_2$ are used to classify athletes (e.g. 14, 16 and 18km.h^{-1} ; (P. U. Saunders, Pyne, Telford and Hawley, 2004b; Barnes and Kilding, 2015) as recreational – elite, but velocity associated with sustaining a high fractional utilisation of $\dot{V}O_{2\max}$ may be a more appropriate individual measure. For example PR ran at $\sim 91\%$ $\dot{V}O_{2\max}$ during her marathon world record (A. M. Jones, 1998; 2006) and demonstrated a 15% improvement in running economy over 11 years (A. M. Jones, 2006), setting the marathon world record too, emphasising that the relative importance of $\dot{V}O_{2\max}$ diminishes and exercise economy increases as event distance/duration increases, as the speed relative to $v\dot{V}O_{2\max}$ also decreases.

A second case series, comparing elite Eritrean and Spanish runners (Lucia *et al.*, 2006) emphasises the interaction of these variables, and the prevailing importance of running economy when $\dot{V}O_{2\max}$ is already high. The Spanish runners displayed greater absolute and relative $\dot{V}O_{2\max}$ values, however the Eritrean group were significantly more economical (i.e. lower $\dot{V}O_2$) at 17, 19 and 21km.h^{-1} , as shown in Table 2.2 below. These paces were chosen as they represent typical training, fast training and racing ($10\text{--}12\text{km}$) velocities for these athletes. Anthropometric characteristics also differed significantly between groups, with Eritreans presenting with lower body mass indexes (BMI), maximal calf circumference and skinfolds than the Spaniards, but possessed greater shank lengths. Simply, Eritreans were lighter, leaner and had a smaller lower limb mass distributed over a greater area; all of which may impose mechanical advantages that reduce the oxygen cost of running. This was further evidenced by higher finishing positions and greater participation at the 2004 and 2005 World Cross Country Championships by the Eritrean

compared to the Spanish athlete(s). For further comprehensive reviews of running economy, the reader is directed to Saunders *et al.*, (2004a) and Barnes and Kilding (2015).

Table 2-2 Maximal Oxygen Uptake and Running Economy values for Elite Eritrean and Spanish runners, adapted from Lucia *et al.*, (2006). Use of asterisk* denotes statistical significance ($p < 0.05$); double asterisk** denotes $p < 0.01$. All values are reported as relative oxygen uptakes ($\text{ml.kg}^{-1}.\text{min}^{-1}$) unless otherwise stated.

	Eritrean	Spanish
$\dot{V}\text{O}_{2\text{max}}$ (absolute; L.min^{-1})	4.2 ± 0.3	$4.7 \pm 0.4^*$
$\dot{V}\text{O}_{2\text{max}}$ (relative)	73.8 ± 5.6	$77.8 \pm 6.1^*$
$\dot{V}\text{O}_2$ at 17km.h^{-1}	52.5 ± 6.4	$59.7 \pm 3.1^*$
$\dot{V}\text{O}_2$ at 19km.h^{-1}	60.0 ± 4.9	$68.6 \pm 4.8^{**}$
$\dot{V}\text{O}_2$ at 21km.h^{-1}	65.9 ± 6.8	$74.8 \pm 5.0^*$

As exercise duration increases to moderate durations (15 min – 2 h), and the intensity remains relatively close to running speeds that elicit $\dot{V}\text{O}_{2\text{max}}$ i.e. a high % $v\dot{V}\text{O}_{2\text{max}}$, the muscle's ability to tolerate and meet these demands aerobically (generation of ATP from lipids) is challenged. This leads to an increased contribution from glycolytic sources (endogenous or exogenous carbohydrate) and in turn elevates blood lactate values [La] and an increase in free H^+ ions within the muscle (Joyner and Coyle, 2008; Hall *et al.*, 2016). Two phenomena ensue, the first is an accumulation of lactate above resting values, and the second an exponential accumulation brought about by maximal exercise intensities (Hall *et al.*, 2016). The terms for these phenomena are inconsistent within the literature, but in a recent review Hall *et al.*, (2016) recommend the terms aerobic lactate threshold and maximal lactate steady state (MLSS) respectively, but the anaerobic lactate threshold is also used. For consistency, aerobic and anaerobic lactate thresholds are the preferred terms within this thesis. Whilst there is now plentiful literature which employs the term MLSS, this is arguably a misnomer as attaining this intensity/velocity elicits a change within the muscle that is in part uncompensable, despite being modelled on a point of metabolic equivalency (Heck *et al.*, 1985; Smekal *et al.*, 2011). This is further complicated when one considers the rate of [La] appearance (R_A) and rate of disappearance (R_D) can be measured, so one may assume a further definition of the anaerobic lactate threshold is when $R_A > R_D$ (Messonnier *et al.*, 2013). This is supported by a rightward shift in a [La] curve during incremental exercise tests being associated with improved endurance exercise capacity (Midgley, McNaughton and Wilkinson, 2006; Ferguson *et al.*,

2018). Values of 2mmol.L⁻¹ and 4mmol.L⁻¹ have also been used to describe aerobic and anaerobic lactate thresholds respectively (Fabre *et al.*, 2013), although individualised models are to be encouraged, these values are typically used by coaches as benchmarks for associated exercise intensities (Hall *et al.*, 2016).

In summary, a high $\dot{V}O_{2max}$ is requisite for elite endurance performance, with running economy a key differentiator of performance between those with similar $\dot{V}O_{2max}$ values. The ability to meet the demands of competition with minimal [La] accumulation is advantageous, so a well-developed anaerobic lactate threshold is also deemed beneficial. Practically this enables an elite runner to sustain a high running velocity by consuming a lower volume of oxygen and lower circulating [La] in comparison to lesser or untrained counterparts who may fatigue earlier due to limitations in one or all of these components. This interrelationship has previously been defined as a formula for marathon performance by Joyner as:

$$\dot{V}O_{2max} \times \text{lactate threshold} \times \text{running economy} \quad (\text{Joyner, 1991})$$

This interrelationship is event specific. Jones (2006) divides events into short-endurance (800-1500m), long-endurance (5000m, 10000m and marathon) and ultra-long endurance (ultra-marathons) categories. Each of these groups is likely limited by differing factors, as evidenced in two classic works (Costill, 1970; J. Daniels and N. Daniels, 1992), and Jones' case studies of PR (Jones 1998; 2006). Daniels and Daniels (1992) noted high $\dot{V}O_{2max}$ values in all athletes tested, irrespective of gender or competitive distance however both genders reported the highest values for those events which lasted the same duration as typical step or ramp protocols used to elicit $\dot{V}O_{2max}$ and whose intensities most closely mirror $\dot{V}O_{2max}$ (Table 3), namely the 3000m – 10000m runners. Costill (1970) demonstrated a clear inverse curvilinear relationship between event distance/duration and [La] values in athletes covering short endurance – ultra-long endurance (Jones, 2006), which is attributed to the event's % $\dot{V}O_{2max}$ requirement and increased aerobic contribution as distance increases (D. W. Hill, 1999; Spencer and Gastin, 2001; Duffield, Dawson and Goodman, 2005; 2007). Finally, Jones case studies provide a unique longitudinal assessment of this interrelationship, as training accumulates, physiology adapts and the manifestation of this was numerous accolades culminating in a marathon world record (A. M. Jones, 1998; 2006).

Table 2-3 VO₂max values of elite distance runners, adapted from Daniels and Daniels (1992). All values are relative to bodyweight (ml.kg⁻¹.min⁻¹)

Group	Male	Female
800m – 1500m	72.5	63.1
3000m – 10000m	77.4	68.4
Marathon	74.4	68.1

2.3.2.2 Structure and function

The previous section extended upon earlier discussion regarding respiratory and metabolic factors that may impact upon and limit endurance exercise performance. This section will focus upon the phenotypic factors that may be advantageous towards endurance exercise performance, or may manifest because of life-long endurance training. The absence of these factors does not necessarily accelerate fatigue, however athletes that display these characteristics may be better protected against fatigue. From an evolutionary perspective, many *Homo sapiens* will display the traits discussed in this section but some display a more extreme phenotype relative to the population.

Anthropometrically humans display a range of adaptations that are beneficial in countering fatigue. A recent comprehensive investigation of factors associated with running economy demonstrated that having examined a plethora of anthropometrical, biochemical, biomechanical and physiological variables only bodyweight was associated with improvements in running economy, and explained 94% of the variance in running economy observed (Lundby *et al.*, 2017). No variables were correlated to cycling economy following multiple regression (Lundby *et al.*, 2017). This highlights the complexity of endurance performance and the variability between individuals' characteristics that produce performance but the rigour of the statistical approach may have limited the authors' findings, as only variables that were linearly related to performance were included in the multiple regression model (Lundby *et al.*, 2017). This investigation also assessed a wide range of participants with respect to $\dot{V}O_{2\max}$ (45.5 – 72.1 ml.kg.min⁻¹), whilst this is commendable, given an appropriate sample size, such a heterogeneous sample with respect to aerobic fitness is likely to produce clusters of data, as what limits an individual with a $\dot{V}O_{2\max}$ of 45.5 ml.kg.min⁻¹ will differ from those recording 72.1 ml.kg.min⁻¹.

Anthropometrically, humans that are better suited to endurance running display common morphological traits such as a relatively smaller than average stature (males), high degree of linearity and a high body surface area to mass ratio (cm²/kg; (Lundby *et al.*, 2017)). Thermoregulatory advantages may also be conferred and are supported further in humans

by possessing less body hair than other primates (Jablonski, 2004), possessing an increased rate of evaporative cooling (Wheeler, 1991) and minimising solar radiation exposure through bipedalism (Wheeler, 1991). Conversely, humans are the fattest of all ape species (Navarrete, van Schaik and Isler, 2011; Zihlman and Bolter, 2015), but this adiposity provides an energy dense fuel depot. These factors are thought to be evolved in part through our species' pursuit of persistence hunting (Bramble and Lieberman, 2004), and as such economic locomotion, fuel availability and thermoregulation were necessary traits for survival. An economical athlete's mass is also distributed closer to the centre of gravity, ensuring a lighter distal mass and decreasing the moment arm through the swing phase of a runner's gait (P. U. Saunders, Pyne, Telford and Hawley, 2004a; Barnes and Kilding, 2015).

There are further biomechanical variables that support economical locomotion in human endurance athletes, these factors are not reviewed exhaustively here, so the reader is directed to pertinent reviews by Saunders (P.U. Saunders *et al.*, 2004a), Barnes & Kilding (2015), Moore (2016) and Bramble & Lieberman (2004).

Working from the ground upwards, in the plantar fascia and Achilles tendon, runners are supported by structures that are capable of rapidly storing and transmitting energy. Wiesinger and colleagues demonstrated structural and energetic property differences between patellar and Achilles tendons in runners and controls (Wiesinger *et al.*, 2017). Moderate differences (η^2 : 0.17) were seen in the Achilles between groups with runners ($4340 \pm 822\text{N}$) demonstrating 11% greater force production than controls (3900 ± 690), and a 30% reduction in hysteresis ($11.8 \pm 3.1\%$ vs. $17.3 \pm 5.1\%$; η^2 : 0.25), suggesting a higher energy storage capacity of tendons in runners compared to controls, that is adaptive and acquired in response to longitudinal training.

Progressing to the knee and associated musculature, Verheul (Verheul, Clansey and Lake, 2017) found similar mechanical differences between training statuses within low and high mileage runners as Wiesinger did between runners and controls (Wiesinger *et al.*, 2017). High mileage runners ($>45\text{km}\cdot\text{week}^{-1}$; mean volume: $68 \pm 17 \text{ km}\cdot\text{week}^{-1}$) when compared to low mileage runners ($<15\text{km}\cdot\text{week}^{-1}$; mean volume $12 \pm 3 \text{ km}\cdot\text{week}^{-1}$) displayed decreased muscular activation at the rectus femoris, semitendinosus and vastus medialis ($p < 0.001$) activity than low mileage runners. The low mileage runners also displayed a 44% greater muscle co-activation ratio at the fastest running speed ($5.5\text{m}\cdot\text{s}^{-1}$). The groups displayed different kinematic and kinetic landing characteristics among all three landing phases ($p < 0.001$). High mileage runners possessed greater knee flexion at higher running speeds (4.5 and $5.5\text{m}\cdot\text{s}^{-1}$), decreased stance time and knee range of motion at lower running

speeds (2.5 and 3.5m.s⁻¹) , greater knee stiffness at initial contact and lower knee stiffness at weight acceptance across all velocities, and performed less negative work and more elastic work (all $p<0.05$) at the ankle across all velocities than low mileage runners. These findings emphasise that training volume is a key determinant of the kinematic and neuromuscular properties of runners, and these adaptations likely contribute to faster running speeds. More simply, high mileage runners preload pertinent muscles through anticipatory neuromuscular activation; this results in greater joint stiffness and elastic energy return when the foot is in contact with the ground, with greater differences between training statuses as velocity increases (Moore, 2016; Verheul, Clansey and Lake, 2017). This work is extended by Tam and colleagues, who assessed similar characteristics and found that the same pattern of neuromuscular activation described above (lower ankle and greater knee stiffness) was associated with a lower oxygen consumption ($R=0.527$ and 0.384 , respectively (Tam *et al.*, 2019)).

These differences are not reported when one examines differences between elite populations (Eritrean vs. Spanish), despite differences in $\dot{V}O_{2max}$ and running economy (Lucia *et al.*, 2006; Santos-Concejero *et al.*, 2015) these differences are not explained by biomechanical parameters, and may only be partially explained by phenotypic adaptations e.g. smaller calf circumference ($R=0.554$; $R^2= 0.307$; (Lucia *et al.*, 2006)). This is further supported by Tam *et al.*, (2016) who only associated improved running economy with rectus femoris – biceps femoris coactivation at 20km.h⁻¹ in elite Kenyan athletes, despite positive associations with knee stiffness during pre-activation and ground contact (Tam *et al.*, 2016).

Finally at the hip and gluteal region, utilising a computer modelling approach having obtained data from nine trained runners, Dorn and colleagues demonstrate that stride length is primarily driven by activation of ankle plantarflexors up to a velocity of ~7m.s⁻¹, whereas stride frequency can be attributed to increased activation of the posterior musculature (gluteus maximus and hamstrings) and musculature that crosses the hip (iliopsoas, gluteus maximus and hamstrings) are attributed to increase hip and knee accelerations at higher running speeds (Dorn, Schache and Pandy, 2012). The authors note that these activation patterns only occur during steady state running and may not translate to accelerations (Dorn, Schache and Pandy, 2012); whilst this is not always a factor in distance running, movements that mimic the increased metabolic cost of acceleration such as ascending or descending may alter the observed movement patterns and underpinning neuromuscular activation, with minimising vertical oscillation (at higher running speeds) also encouraged (Moore, 2016)

To conclude, the data presented above are interpreted from the perspective that humans have evolved to be ‘good’ distance runners relative to other members of the animal kingdom; this is the central tenet of the endurance running hypothesis (Carrier, 1984; Bramble and Lieberman, 2004) and must be borne in mind when examining factors that limit endurance running performance because what we consider desirable characteristics for sporting performance, more than likely served an evolutionary and genetic advantage, historically.

2.3.2.3 Critical core temperature

Humans, along with nearly all mammals and birds, are *homeotherms* (C. J. Gordon, 2012) and thus the maintenance of core temperature (T_{core}) within a narrow range, above that of the local environment, is considered vital for homeostatic purposes. Exercise in hot conditions causes an elevated rate in the rise of T_{core} and therefore an increase in heat storage that can become deleterious, and may induce heat related illness such as heat stroke, or hyperthermia (define). Contention exists within the literature as to whether a critical core temperature exists, what critical core temperature may be and that the attainment of this temperature is responsible for fatigue. Consideration of the heterogeneity of core temperature at rest provides initial insight into the inherent variability of human temperature and helps to contextualise the notion of a critical core temperature at the point of exercise cessation/termination.

A recent epidemiological study has contested a common baseline temperature for humans (Obermeyer, Samra and Mullainathan, 2017), which has stood at 37°C since Carl Wunderlich’s seminal work, published in 1868 and consisting of a sample of 25000 individuals (Mackowiak and Morgan, 2017). It is argued that due to the relative enormity of this dataset Wunderlich’s conclusion was not challenged, yet 37°C is neither the mean daily temperature, mean temperature at any point, nor the most recorded temperature within individuals (Mackowiak, S. S. Wasserman and M. M. Levine, 1992; Mackowiak and Morgan, 2017). Individual variation in T_{core} may be attributed to a range of factors such as age, biological sex, ethnicity and menstrual cycle stage (K. A. Lee, 1988; Sund-Levander, Forsberg and Wahren, 2002; Kelly, 2006; Waterhouse *et al.*, 2009; Racinais *et al.*, 2019), but these factors may only explain a small percentage of the variance in T_{core} (Obermeyer, Samra and Mullainathan, 2017) and are further susceptible to diurnal variation (Mackowiak, S. S. Wasserman and M. M. Levine, 1992; Waterhouse *et al.*, 2009). This diurnal variation has obvious implications for exercise performance, especially if a critical T_{core} exists, as the temperature one commences exercise at may be

higher or lower and thus the permitted change (ΔT_{core}) relative to the critical threshold may be diminished or increased.

Evidence for a critical mammalian T_{core} originates from a rodent study which demonstrated a commonality in the abdominal and brain temperatures ($\sim 40^{\circ}\text{C}$) attained by exercising rats at the point of fatigue (Fuller, Carter and Mitchell, 1998) despite the implementation of different precooling strategies. In humans, similar observations were seen by Cheung (Cheung and McLellan, 1998), González-Alonso (González Alonso *et al.*, 1999), Nielsen (Nielsen *et al.*, 1993; 1997) and Nybo (Nybo & Nielsen, 2001) who report fatigue as aligning with temperatures approaching 40°C . However, these studies all took place in laboratory conditions that maximise the rate of heat storage of an individual by minimising evaporative cooling (either by no wind speed or increased humidity) and exercising at a fixed intensity (Noakes, 2007). This does not mean they should be completely discredited but their conclusions may not be ecologically valid. Indeed, Byrne and colleagues (2006) assessed a mass participation half marathon (21.1km) race and noted variation in maximum T_{core} attained during exercise, with an upper measure of 41.7°C and a range of $39.3\text{--}41.7^{\circ}\text{C}$ (Byrne *et al.*, 2006). They clarify by stating that all runners attained $T_{\text{core}} > 39^{\circ}\text{C}$, 56% $> 40^{\circ}\text{C}$ and 11% $> 41^{\circ}\text{C}$, clearly indicating that the attainment of an arbitrary critical core temperature is either non-catastrophic, or most likely individual in nature, much like the evidence presented earlier on resting temperature (Obermeyer, Samra and Mullainathan, 2017). Similar maintenance of performance despite elevated core temperatures $> 40^{\circ}\text{C}$ are seen in a simple proof of principle investigation by Ely *et al.*, (2009) who compared the running velocity over the final 600m of 17 athletes (10male; 7 female) participating in an 8km run. The group was divided in two, those with $T_{\text{core}} > 40^{\circ}\text{C}$ and those with $T_{\text{core}} < 40^{\circ}\text{C}$, and no significant difference in mean running velocity was found ($279 \pm 28\text{m/min}$ vs. $282 \pm 27\text{m/min}$ respectively; $p < 0.16$ (Ely *et al.*, 2009)). Whilst a running speed of 3m/min may be considered a practically meaningful difference, this is within the 1.5% coefficient of variation expected of trained distance runners' performance over distances shorter than a half marathon (Hopkins and Hewson, 2001), and so instead may be construed as typical of race to race variation.

Evidence countering the critical T_{core} concept has most recently been supported by Racinais during the UCI World Cycling Championships (Racinais *et al.*, 2019) in which 10 of 40 riders attained temperatures $> 40^{\circ}\text{C}$, and two cyclists exceeded 41°C . The authors also note that the rate of temperature accumulation and maximum temperature attained are event specific; road races produce lower peak temperatures than team and individual time trials, irrespective of sex, most likely due to differences in exercise intensity and pacing

profiles between events. It is noted that in the road race, as power increased in the final section of the race, T_{core} transiently reduced, with an increase in convective and evaporative cooling due to faster cycling speeds (Racinais *et al.*, 2019).

For the purpose of this thesis, the concept of a critical T_{core} is considered as highly individual with respect to a maximum value and displaying intra-individual variation based upon prior heat exposure, training status and the use and nature of cooling methodologies. The rate of heat accumulation, and the $T_{\text{core}}:T_{\text{skin}}$ gradient may be more potent drivers of fatigue than the attainment of an arbitrary cut off point, evidence for these factors are presented in subsections 2.4.1.2 and 2.4.1.3, and it is likely the integration of these physiological markers that manifest in an athlete's being too hot to continue exercising.

2.3.3 Integrated approaches to fatigue

Fatigue may be described as a non-homeostatic event across one or more biological systems. Integrated approaches to fatigue present explanations for fatigue by acknowledging that one system is not solely attributable for the onset of fatigue, but that fatigue can be attributed to deviation from homeostasis across a range of hierarchical biological systems at any one time. The following sections explore integrated models of fatigue with respect to sport and exercise performance, with Section 2.3 concluding by using ultra-endurance running as an example of integrated approaches to fatigue in action.

2.3.3.1 Rating of Perceived Exertion: Gestalt and Differential perspectives

The investigation of rating of perceived exertion (RPE) is most credited to the Swedish psychologist Borg. Borg has presented scales of perceived exertion (G. Borg, 1998; E. Borg and G. Borg, 2002; E. Borg *et al.*, 2009) which aim to capture the degree of strain caused by task completion across all systems (physiological or otherwise) involved in producing the performance in question. Despite widespread use, mistakes in nomenclature are reportedly common, and administration may differ between laboratories (Abbiss *et al.*, 2015) but perhaps the most important misinterpretation is that which occurs when describing perceived effort and perceived exertion. Hutchinson and Tenenbaum (2006) differentiate between these factors by stating that perceived effort is the perception of work exerted by the exercising participant to complete the task, whereas perceived exertion is the sensation(s) elicited by and at the time of performing the task (Hutchinson and Tenenbaum, 2006). Abbiss (2015) presents this more succinctly, effort is 'the amount of

physical or mental energy being given to a task’, whereas exertion is the ‘degree of heaviness and strain experienced in physical work’ (G. Borg, 1998; Abbiss *et al.*, 2015).

The presented definitions of exertion align with the idea of interoception detailed below in section 2.3.3.2, however, despite its ubiquity in sport and exercise science, Borg’s concept of perceived exertion as a singular parameter that encompasses the exertion experienced during exercise has been meaningfully critiqued. Opting for a single measure of exertion makes little sense, when one considers the complex interplay of neurology, physiology and psychology that interact with higher order processing to answer the question ‘How did that feel?’ upon exercise termination.

Hutchinson and Tenenbaum (2006) put forth an experimental critique of Borg’s model with the aim of ascertaining whether RPE can be considered a gestalt measure, or whether it is best assessed via a differential approach. The authors tested two groups of participants’ performances on two sustained exercise tasks involving different muscle groups and assessed their perceptual responses across three dimensions of effort: sensory-discriminative, motivational-affective, and cognitive-evaluative. It was hypothesised that participants would experience these dimensions differently, and this was supported as dimensions displayed differing magnitude and time responses during each exercise bout (Hutchinson and Tenenbaum, 2006), similar to earlier findings by the same group (Tenenbaum *et al.*, 1999). Whilst these studies have grouped sensations into dimensions, where possible it may be prudent to capture sensations at the level of individual afferent sensory inputs, as these are interpreted by differing regions of the brain before further processing (A. D. Craig, 2002; 2009), for instance Tenenbaum *et al.*, (1999) originally investigated responses to running performance across eight sensory factors: proprioceptive symptoms, leg symptoms, respiratory difficulties, disorientation, dryness and heat, task completion thoughts, mental toughness, and head or stomach symptoms. Upon closer inspection, these factors are often assessed simultaneously and independently during sports science research but the method of assessment differs dependent upon the factor in question, potentially presenting researchers with an apparent tautology between a differential and integrated approach to assessing ratings of perceived exertion.

An example of this may be respiratory frequency (f_R), which is strongly associated with RPE, and mirrors the work performed in a task more closely than commonly assessed variables such as HR, [La] and $\dot{V}O_2$ which display a lag following exercise onset and cessation (Nicolo:2014bt; Nicolò, Massaroni and Passfield, 2017). Furthermore, the mechanism that is thought to regulate f_R is central in nature (Marcora, 2009) and so this variable may act as a physiological proxy for central RPE, if required e.g. in youth athletes

who may have difficulty in expressing RPE values, or may display higher differential RPE values at the same physiological threshold (Mahon, Gay and Stolen, 1998) when compared to adults. This also highlights the importance of embedding RPE assessment into training environments, and using this data in a way that is meaningful to athletes.

Longitudinal investigations of differential approaches to RPE have been completed in team sports (Weston *et al.*, 2014; McLaren *et al.*, 2018) with a view to further elucidate the contribution of differing sensory inputs in athletes' internal load (Weston *et al.*, 2014; Arcos *et al.*, 2016; McLaren *et al.*, 2018). When paired with measures of external load, such as those obtained by global positioning systems, these data present a detailed quantification of the stresses experienced (and interpreted) by an athlete over a given duration (McLaren *et al.*, 2016). Additionally, differential RPE data may support wider interventions with strong physiological bases; Arcos and colleagues state that soccer players who played fewer than 45min presented with increased respiratory ratings of exertion than those who played longer (Arcos *et al.*, 2016). Mechanistically, this may be due to lower levels of muscle glycogen utilisation due to shorter playing time, and may inform post-match nutrition strategies, such as increasing dietary carbohydrate intake (Bangsbo, Mohr and Krstrup, 2006).

These recent data are interesting from an endurance sports perspective as when assessed chronically they may provide an indication as to the time-course of how fitness is acquired and perceived by individuals, how this may differ between training statuses and how this may be influenced by dietary manipulations.

2.3.3.2 Interoception: A Sense of Self

The notion of interoception was honed in 2002 by AD 'Bud' Craig (A. D. Craig, 2002) building upon the earlier mid-century work of Sherrington who suggested that the sense could be codified into teloreceptive, proprioceptive, exteroceptive, chemoreceptive and interoceptive (Sherrington, 1906; A. D. Craig, 2002). Interoception by Sherrington's definition was a sense of visceral occurrence/presence (A. D. Craig, 2002) however, Craig's model sees interoception linked closely with a brain region (the anterior insula cortex) that is involved in the detection and interpretation of thermoregulation and other homeostatic processes that are pertinent to this thesis, such as dyspnoea, heartrate and thirst (A. D. Craig, 2009).

Activation of the anterior insular cortex is underpinned by an elaborate neural network, consisting of both afferent and efferent networks. The breadth and magnitude of stimulation depends upon the stimulus one is exposed to; for instance, a stimulus that is

more arousing such as heartbeat awareness (Critchley *et al.*, 2004), subjective cooling (A. D. Craig *et al.*, 2000) and heat pain (J. C. W. Brooks *et al.*, 2002) stimulate the anterior insula cortex unilaterally, with more emotive stimuli presenting bilaterally (A. D. Craig, 2009) and manifesting as sensations.

These sensations, are thought to originate in the posterior insula cortex and progress anteriorly towards higher order centres of the brain. Neural inputs stimulate the posterior insula cortex and are compared to homeostatic norms which provide the template for stimuli assessment. As the signal progresses forwards to the mid-insular cortex, different brain regions ‘feed in’ depending upon the nature of the stimulus, enriching the signal(s) underpinning motor-functional, environmental and hedonic stimuli before these are affected at a motivational or cognitive level by the anterior insula cortex. In Craig’s 2009 review, this posterior-anterior progression is depicted as a series of bodies, displayed in deepening hues as a colourful representation of more information being layered upon the initial signal/stimulus (A. D. Craig, 2009). These illustrations effectively depict the progression of the interoceptive ‘question’ from a homeostatic template of ‘How I should feel?’ in the posterior insular cortex to ‘How do I feel?’ in the anterior insular cortex.

The interoceptive neural network may be ‘the black box’ the central governor theory has previously described (Ulmer, 1996; Lambert, Gibson and Noakes, 2005; McMorris, Barwood and Corbett, 2018), but advances the central governor theory in the following ways: Firstly, it provides an integrated neural network for the detection and maintenance of multiple physiological systems, and recognises this interconnectedness. Secondly, the biphasic approach of the interoceptive system from detection to interpretation as signals arrive from the periphery into the anterior and progress posteriorly, before moving to the somatosensory cortex (McMorris, Barwood and Corbett, 2018). Finally, it is falsifiable. Stimuli may be presented to an individual and the responses in this neural network measured, ensuring a scientifically stronger model, than the teleological approach presented by the central governor, seemingly ‘knowing’ everything and yet affected by everything (Noakes, 2012).

However, in consciously presenting stimuli to an individual, we may fall victim to the ‘neural spotlight effect’ (Müller and Kleinschmidt, 2007; Hassanpour *et al.*, 2016). This term, used to describe the influence of the awareness of a preceding stimulus upon a subsequent target stimulus (Müller and Kleinschmidt, 2007), has particular relevance to fatigue in sport and exercise, as we can prime an athlete’s (thermoregulatory) system with a plethora of stimuli from the presence of competition (Corbett *et al.*, 2017), to deception of thermoregulatory state (Castle *et al.*, 2012; D. N. Borg *et al.*, 2018) and absence of

nutrient availability (Che Muhamed *et al.*, 2014). Indeed, such priming effects have been examined from an interoceptive neurological perspective with respect to emotional state (Paulus and Stein, 2010; Zaki, Davis and Ochsner, 2012; Grupe and Nitschke, 2013) and heartrate (Critchley *et al.*, 2004; Pollatos *et al.*, 2007), with accompanying preliminary (i.e. non-brain imaging) work assessing the relationship between ventilatory awareness and anxiety (Faull, Cox and Pattinson, 2016).

A consciously interoceptive approach may be limited in terms of application to sport, however. There is a preponderance of literature assessing the effects of an external attentional focus on skill-dependent activities such as golf (Hüttermann, Memmert and Simons, 2014) and may also be beneficial in simpler tasks such as walking or running (Wulf, 2013). The benefits of adopting an external focus is that it shifts focus away from interoceptive systems and symptoms and allows the performer to focus solely on the process(es) required to produce a successful task outcome (Wulf, 2013; Hüttermann, Memmert and Simons, 2014). In this instance, interoception would still occur but would be a subconscious process as opposed to an active part of the cognition required to execute the task. Counterintuitively, data from fMRI (Critchley *et al.*, 2004; Pollatos *et al.*, 2007) and Transcranial Magnetic Stimulation (Kuhn *et al.*, 2016) support that the insular cortex experiences increased activity when an external focus is adopted, suggesting that despite this process not being aware of interoceptive processes, the interoceptive neural network still generates, adjusts and responds to a template.

Motivation also warrants consideration with respect to interoception and the resultant behavioural outcomes it generates. Hypothetically, if an athlete is highly motivated they may further challenge interoceptive feedback and systems, especially if rewards are high and core temperature is perceived not to be. This may have serious side effects, such as increasing the risk of heat death and inducing heat illness or, simply permit the athlete to win the race and recover normally. We may see these effects worsened in recreational athletes who likely do not possess the interoceptive and thermoregulatory abilities of elite athletes, but may be no less motivated due to economic or time investments into a task e.g. an ultra-marathon or multi-day event. In contrast, an increased motivation under greater interoceptive and or physiological stress may lead to the adoption of task pacing strategies (McMorris, Barwood and Corbett, 2018).

2.3.3.3 Integrative model for hyperthermia induced fatigue

A model of integrative hyperthermia induced fatigue was proposed by Nybo and colleagues (Nybo, Rasmussen and Sawka, 2014) in their comprehensive review of

physiological factors associated with hyperthermia induced fatigue. The model depicts how the combined influences of changes within cardiovascular, neurobiological, muscular, psychological and respiratory systems during performance in hyperthermic conditions, manifest in fatigue. The authors rightly acknowledge that literature tends to be orientated towards single parameters as potential explanations for fatigue and exhaustion, hence their proposal of a model that accounts for the interaction between multiple systems during exercise inducing fatigue. However, it is important to note that the dominant limiting system and relative importance of supporting systems may differ dependent upon exercise intensity, duration or mode (Nybo, Rasmussen and Sawka, 2014) and an athlete's state of physiological (section 2.2.1) or psychological preparedness (section 2.2.2), as well as hyperthermia specific factors such as the heat transfer characteristics of the exercise task (as per Figure 2.2) and exercise environment (section 2.2.3).

Nybo *et al.*, 's (2014) model provides an appropriate summary of the models of fatigue discussed in this chapter, acknowledging roles for psychological and physiological constituents of fatigue, whilst accepting that fatigue is most likely multifactorial in nature. Unfavourable environmental and heat transfer characteristics clearly accelerate the process of fatigue across most systems, inducing a hyperthermic state within the athlete; the extent and time course of which is dependent upon each system's readiness, which will also differ between athletes of varying competitive abilities and specialties.

2.3.3.4 Lessons from Ultra running

Ultra-running serves to highlight that whilst fatigue may be multi-factorial and manifest in differing ways within and between individuals, fatigue is not solely peripheral; nor is it solely central, therefore, an integrated model should be favoured by practitioners and researchers. The interactive nature (Best, Barwick, *et al.*, 2018) of contributory factors to fatigue during prolonged running suggest that fatigue in this context is not task but state dependent, in that an ultra-runner's interpretation and manifestation of fatigue is represented across a spectrum of variables with differing time courses as running distance/duration increases (G. Y. Millet, 2011; G. Y. Millet, Banfi, *et al.*, 2011; G. Y. Millet, Hoffman and Morin, 2012; G. P. Millet and G. Y. Millet, 2012; Lazzer *et al.*, 2012; Kerhervé, G. Y. Millet and Solomon, 2015; Best, Barwick *et al.*, 2018). This notion is explored, and subsequently applied through a return to standardised middle and long distance running events.

This position is highlighted by several authors, across a range of study designs. Firstly, in a recent case study, assessing the between race variability of subjective metrics and

nutritional status, Best (Best, Barwick, *et al.*, 2018) found that subjective variables interact and display differing time courses within an individual, potentially limiting performance by doing so. In this instance performance was enhanced to the degree of event completion when pain was mitigated; however, in the failed attempt pain rose substantially and independently of rating of perceived exertion, whilst presenting as inversely proportional to feelings of freshness and motivation (Best, Barwick, *et al.*, 2018).

Secondly, work by Guillaume Millet and Stefano Lazzer details the time course of fatigue in ultra-running across various event durations and technical difficulties (G. Y. Millet, 2011; G. Y. Millet, Banfi, *et al.*, 2011; G. Y. Millet, Hoffman and Morin, 2012; G. P. Millet and G. Y. Millet, 2012; Lazzer *et al.*, 2012; Kerhervé, G. Y. Millet and Solomon, 2015). These papers methodically outline the fatigability of (neuro-)musculature, corresponding physiological and concomitant subjective responses. Whilst highlighting the individualised and interconnected nature of fatigue these papers also serve as a useful reminder that fatigue ‘exists’ predominantly in the method used to assess it, whether this has a central emphasis or otherwise. Millet notes that despite ultra-running now being a predominantly recreational pursuit (G. Y. Millet, 2011) central, mechanical and structural robustness developed in response to prolonged running is likely responsible in part for shaping our predecessor, *Homo erectus* (Bramble and Lieberman, 2004; Lieberman and Bramble, 2007), and thus irrespective of its presentation, fatigue is of evolutionary importance.

Thirdly, in the Trans Europe footrace which covers 4487km, Freund and colleagues demonstrated that in most runners the event generated potentially adaptive osteogenic and tendon responses, with a small number experiencing oedema and plantar fascia issues (Freund *et al.*, 2012). In the same cohort Freund also noted that pain tolerance is much higher, but it is noted that this tolerance may be a consequence not a cause of prolonged distance running (Freund *et al.*, 2013). Both findings have bearing upon fatigue, as the extreme exercise duration required to participate in and complete these events requires a body and mind that can tolerate prolonged running over successive days.

Fatigue in the context of ultra-running may appear to be a process of attrition, whereby athletes manage physiological resources and psychological load, employing mitigation strategies, such as performance nutrition which may actively combat fatigue (Costa, Hoffman and Stellingwerff, 2018; Hoffman, Stellingwerff and Costa, 2018). Whereas shorter distance events (e.g. <half marathon/21.1km) may still be contested in a time trial like fashion and present a faster time course of fatigue, whilst a well-honed interoceptive network is crucial to success at the elite level, if an appropriate fatigue template is not

generated symptoms of fatigue are likely accelerated more quickly, due to elevated metabolic and thermoregulatory requirements of running at >20 km/h.

2.4 Heat as a driver of fatigue

As identified in section 2.2.3.3, heat is a powerful driver of fatigue and typically reduces performance in comparison to performance in temperate environmental conditions. There are several responses that underpin this global reduction in physiological output, which also alter accompanying perceptual variables. The following sections detail these outcomes in isolation for adequate illustration and scrutiny. It should be borne in mind though that these systems, whilst displaying different response time courses, accumulate to limit endurance exercise performance collectively, and an elevation in one system may lead to a downregulation in another, and vice versa, but performance would still be impaired.

2.4.1 Physiological effects and responses

2.4.1.1 *Inhibition and habituation of central factors*

Central factors may be impaired due to acute endurance exercise performance in the heat, however it seems that exercise needs to be of a sufficient duration to for this to occur. This highlights the likely role of increased T_{core} in the inhibition of central drivers of performance (Ftaiti *et al.*, 2001; Racinais and Oksa, 2010) as time is required for T_{core} to become elevated.

To assess the relationship between temperature and neuromuscular activity, Ftaiti and colleagues (2001) performed a quite contrived experiment, whereby they maximised the rate of heat storage of athletes by having them exercise at 65% $\dot{V}O_{2max}$ for 40 min, whilst wearing a non-permeable tracksuit. Prior to and immediately post-exercise participants' knee extension and flexion torques were assessed at 60 and 240°.s⁻¹, with EMG recorded throughout. Participants reported elevated temperatures ($40.0 \pm 0.3^{\circ}C$) and demonstrated a reduction in torque and EMG activity during the slow (60°.s⁻¹) but not the fast (240°.s⁻¹) component, suggesting endurance may be impaired but fast contractions may not be. Tucker (Tucker *et al.*, 2004) showed a similar inhibition of 20km cycling performance in hot conditions, as participants could only sustain ~25-30% MVC in hot (35°C) conditions compared to 30-45% MVC in cool (15°C) conditions. Participants in cool conditions also demonstrated a clear 'end spurt' as expressed by change in %MVC and power output, but this was largely absent from trials in the heat, which also showed a reduction in power

output at 80% of trial duration. Again, T_{core} was elevated in the heat to a final T_{core} of $39.2 \pm 0.6^{\circ}\text{C}$, emphasising the role of an elevated temperature exacerbating a reduction in central output. Time trial performance ($p < 0.05$) and power output ($p < 0.01$) were worse in the heat than in cool conditions; we can be somewhat confident that this time difference between trials of 48 seconds or 2.7% is meaningful as participants were classified as performance level 3 (De Pauw and Roelands, 2013) and the change exceeds typical coefficient of variation of cycling time trial performance (Paton and Hopkins, 2006).

Central factors can acclimate to heat however, and these effects may also be exercise stimulus specific. Wingfield *et al.*, (2016) demonstrated differential responses in MVC and associated variables to short term heat acclimation (five days; $32.0 \pm 1.6^{\circ}\text{C}$) depending upon exercise duration and intensity (Wingfield *et al.*, 2016), in performance level 1 athletes ($\dot{V}\text{O}_{2\text{max}} < 45\text{ml.kg.min}^{-1}$; (De Pauw and Roelands, 2013)). When a 30 min high intensity stimulus was applied participants improved sprint power output (5.6%) and maintained MVC, whereas 90 min low intensity (40% W_{max}) exposures impaired MVC but improved 20km cycling time trial performance in comparison to the 30 min high intensity group. Whilst the notion of undertaking an intensity personalised heat acclimation strategy to mitigate the effects of central fatigue in hot conditions is appealing, a combination of both high and low intensity sessions is likely the most advantageous for an athlete, so that time at high T_{core} is also accumulated as well as efforts sport specific intensities.

2.4.1.2 Brain Temperature

The temperature difference between the aorta and jugular venous blood supplies is typically 0.3°C ; during exercise associated hyperthermia this is reduced to 0.2°C suggesting that the brain undergoes a heat storage response in line with aortic blood temperature, and is at least $0.2^{\circ}\text{C} > T_{\text{core}}$ (Nybo, Secher and Nielsen, 2002; Nybo, 2012). Lowering brain temperature during exercise in humans may not be possible, even when seemingly targeted mechanisms such as neck cooling are employed (Tyler, Wild and Sunderland, 2010; Nybo, 2012; Tyler, Sunderland and Cheung, 2013; Bright *et al.*, 2019) due to the relatively minimal amount of contact area and therefore opportunity for heat transfer between (aortic and venous) blood supply and the cooling intervention, which is exacerbated due to a reduction in brain blood flow concomitant with the increase in brain temperature (Nybo *et al.*, 2002; Nybo, Secher and Nielsen, 2002; Nybo, 2012). Oesophageal cooling through ice slurry ingestion may present an alternative to neck cooling (Siegel and Laursen, 2012) due to the close proximity of the oesophagus and

carotid arteries (Mariak *et al.*, 1999; Siegel and Laursen, 2012), yet Nybo (2012) suggests that despite cooling strategies such as face fanning lowering tympanic membrane temperature (Nybo, Secher and Nielsen, 2002) practitioners' efforts are best directed towards lowering T_{core} as arterial and venous blood temperatures remain elevated.

2.4.1.3 Core Temperature

Core temperature (T_{core}) is reported as being consistently elevated following exercise in the heat. This elevation is brought about by a mismatch between the rate of heat loss and heat storage and can be expressed using the following equation (Kenny and Jay, 2013):

$$(M - W) = (H_{dry} + H_{evap} + H_{resp}) + S$$

Where M is metabolic rate and W is work performed, thus $(M - W)$ is metabolic work. All H elements are methods of heat dissipation; H_{dry} is dry heat transfer and is the accumulation of heat lost through conduction, convection and radiant heat loss. H_{evap} is heat lost through evaporation due to differences in partial pressure of liquid on the skin's surface relative to the local environment and H_{resp} is heat lost through respiration, the rate of which is determined by pulmonary ventilation (Kenny and Jay, 2013). Finally, S represents the rate of heat storage and is driven by an imbalance between heat production $(M - W)$ and heat loss $(H_{dry} + H_{evap} + H_{resp})$. Through examination of the above equation it is easy to see that exercise in the heat results in a clear mismatch between rates of heat loss and heat storage, especially if humidity is also high. The relative intensity of exercise performance determines the rate of heat accumulation (Mora-Rodriguez, Del Coso and Estevez, 2008) and thus has been recommended as a predictive factor for those looking to purposefully increase T_{core} for activities such as heat acclimation strategies (O. R. Gibson *et al.*, 2016).

Heat accumulation during exercise can be potentially fatal (Casa *et al.*, 2015), with an increased awareness of the prevalence of exertional heat illness sustained during exercise, especially in student athletes (Casa *et al.*, 2015; Rodgers, Slota and Zamboni, 2018). The role of a critical core temperature ($\sim 40^{\circ}\text{C}$) in fatigue is discussed in section 2.3.2.3. Adopting a uniform critical core temperature of 40°C may be a dubious assumption, as elite level cyclists (Racinais *et al.*, 2019) and race walkers (Stevens, unpublished observations) demonstrate temperatures $>40^{\circ}\text{C}$ in competition. These data are supported by Ely and colleagues in competitive runners who showed $T_{core} > 40^{\circ}\text{C}$ in 12 of 17 runners (B. R. Ely *et al.*, 2009), and Byrne in 10 of 18 recreational runners, reporting a peak value in one athlete of 41.7°C (Byrne *et al.*, 2006).

Strategies to mitigate increased T_{core} during exercise are outlined in section 2.5, but perhaps the most interesting finding with respect to T_{core} is that when ice slurry is ingested to prophylactically lower T_{core} prior to exercise, at the point of exercise termination athletes who ingested ice slurry may report a higher T_{core} than those who did not due to an increased metabolic work output (Siegel *et al.*, 2010), potentially delaying recovery from an exercise bout. This would be exceptionally important in events that require performance in hot environments on consecutive days such as La Vuelta a España or Rugby Sevens tournaments (L. Taylor *et al.*, 2018), and may suggest a role for cooling strategies that target the peripheral temperature of an athlete as well as T_{core} .

2.4.1.4 Peripheral/ Skin Temperature

As with T_{core} , peripheral or skin temperature (T_{skin}) increases as exercise intensity or duration in the heat increases (Tucker *et al.*, 2006; Siegel *et al.*, 2010; Schlader, Simmons, Stannard and Mündel, 2011a; Levels *et al.*, 2012; Cuddy, Hailes and Ruby, 2014; Rendell *et al.*, 2017; Willmott *et al.*, 2018). This is due to an increased rate of blood flow to the periphery which increases the gradient between the environment and skin vapour pressure to facilitate H_{evap} . This higher rate of perfusion aims to lower T_{core} (Maughan, 2010) or at least modify the core to skin temperature gradient, which has been considered as a driver of fatigue (Cuddy, Hailes and Ruby, 2014) to the effect of a 1.5% performance impairment per 1°C T_{skin} increase (Sawka, Cheuvront and Kenefick, 2012). Minimising the T_{core} to T_{skin} gradient and reducing the potential for H_{evap} by wearing additional clothing has recently been explored as a method of heat acclimation (Stevens *et al.*, 2018; Willmott *et al.*, 2018); this intervention successfully increases T_{skin} due to the previously stated mechanisms, but sweat rate also increases (Stevens *et al.*, 2018; Willmott *et al.*, 2018) which has the potential to decrease cardiac output (\dot{Q}) and accelerate dehydration, subsequently impairing endurance exercise performance.

2.4.1.5 Sweat Rate

When exercising in the heat, athletes demonstrate an increase in sweat rate than in cooler conditions (Sawka, Cheuvront and Kenefick, 2012), with fitter athletes also demonstrating an earlier onset of sweating in hot conditions than lesser trained counterparts (Cheung and McLellan, 1998). An increased sweat rate aims to decrease the rate of heat storage by diverting temperature away from the core, and towards the periphery, this is driven by an increased cutaneous vasodilation, effectively increasing the rate of perfusion of the skin. In doing so we predominantly see an increase in the evaporative heat loss (H_{evap}) as the

partial pressure of liquid on the skin (sweat) may exceed that of the local environment (humidity) and because of this pressure gradient, evaporation occurs.

The ability to dissipate heat via H_{evap} clearly becomes compromised in humid environments, where the moisture content of the local environment may exceed the rate of H_{evap} ; thus, the water pressure gradient is reduced between the skin and environment and a local heat storage response occurs at the skin, which in turn elevates T_{core} as blood, originating from working musculature, cannot be cooled sufficiently. This can be partially combatted by H_{dry} which may be altered as a result of wind speed (A. G. Saunders *et al.*, 2005), clothing (Stevens, 2018; Willmott *et al.*, 2018) or performance velocity (Nybo, 2010; Mora-Rodriguez, Ortega and Hamouti, 2011) but performance will ultimately be limited if the rate of heat production ($M - W$) and the environmental conditions exceed the individual's ability to dissipate heat (Kenny and Jay, 2013). This is exemplified in the case study of Alberto Salazar competing in the 1984 Los Angeles Olympic Marathon (Armstrong, Hubbard, *et al.*, 2016), during which Salazar lost 8.1% of his bodyweight (5.43kg) over 134 minutes of running equating to a sweat rate of $>3L.h^{-1}$. This occurred despite fluid provision throughout the race and conditions that were below the human thermoneutral zone (23.9-27.8°C dry bulb), facilitated H_{evap} (wind speed: 2.2-5.4m.s⁻¹) but with high humidity (75% (Armstrong, Hubbard, *et al.*, 2016)).

Interestingly, if T_{core} increases by 1°C but T_{skin} remains the same, then there is a diversion of blood back to the core or working musculature and skin blood flow is lowered, a worked example is calculated by Sawka *et al.* (2012) as follows: a 38°C T_{core} and a 36°C T_{skin} requires 4.4L.min⁻¹ skin blood flow, but a 39°C T_{core} and a 36°C T_{skin} only require a skin blood flow of 2.9L.min⁻¹ (Sawka *et al.*, 2012). Some of the advantages of this reduction in peripheral blood flow are a reduction in HR for a given temperature due to an improved maintenance of \dot{Q} and $\dot{V}O_{2max}$ (Cheuvront *et al.*, 2010), improved brain blood flow and brain oxygenation during exercise (Nybo and Nielsen, 2001; Nybo *et al.*, 2002; Sawka *et al.*, 2012). The inverse is true with higher T_{skin} , which demonstrates an exponential relationship with HR as T_{skin} elevates $>35^{\circ}C$ (Cheuvront *et al.*, 2003).

Sweat rate is also inextricably linked with hypohydration and percentage bodyweight loss during exercise. Hyponatraemia will not be discussed despite its reported prevalence in mass participation endurance activity (Almond *et al.*, 2005; Hew-Butler *et al.*, 2015), as heat ($>28^{\circ}C$) will likely increase sweat rate to offset fluid consumption in that context, managing risk of occurrence.

Hypohydration has been shown to decrease performance (Cheung and McLellan, 1998; Castellani *et al.*, 2010; Kenefick *et al.*, 2010; P. Watson *et al.*, 2015; Funnell *et al.*, 2019)

and is typically considered to be deleterious from ~2% bodyweight loss in laboratory settings (Montain and Coyle, 1992), which can be assessed simply as a urine colour ≥ 5 on the urine colour chart (McKenzie, Munoz and Armstrong, 2015). The magnitude of performance deficit sustained depends also upon environmental temperature (Kenefick *et al.*, 2010; Sawka *et al.*, 2012), as Kenefick and colleagues showed a greater performance deficit during a 15 min time trial as temperature increased (10°C, 20°C, 30°C, 40°C), showing performance decrements $>CV$ from 20°C. This is interesting as it not only suggests that performance can be impaired due to hypohydration in relatively mild temperatures (20°C) but suggests that performance may not worsen outside of CV in cool conditions (10°C) because of hypohydration. As this low temperature range is considered optimal for marathon running (Maughan, Watson and Shirreffs, 2007; Kenefick, Cheuvront and Sawka, 2007; M. R. Ely *et al.*, 2008; Maughan, 2010; Helou *et al.*, 2012), it is not unreasonable to suggest that a small reduction in bodyweight and accompanying provision of fluids during the race, may improve performance because of enhanced exercise economy. This is supported by at least three separate investigations. Firstly, Zouhal and colleagues demonstrated that in a sample of 643 marathon runners, those runners who attained a faster finishing time showed a significant relationship bodyweight loss, especially in those who completed the marathon in <3 h, who demonstrated bodyweight losses of $>3\%$ on average (Zouhal *et al.*, 2011). The authors conservatively concluded that drinking *ad libitum* during a marathon permits a greater reduction in bodyweight but may also be ergogenic. This is supported by a meta-regression from Goulet (2011), that found that athletes performing self-paced time trials in outdoor conditions experienced hypohydration up to 4% bodyweight loss, and that this was not deleterious to performance. The greatest improvements in power output (2-8%) were seen between 1-2% bodyweight loss, but these results should be treated cautiously as only seven studies, with low sample sizes (6-10 participants), across a range of temperatures were included in the analysis (Goulet, 2011). The authors do present a funnel plot to assess publication bias, but there are an equal number of positive and negative responses as a result of hypohydration. Taken together these findings suggest that whilst exercised induced hypohydration may not impair performance, the response is likely highly individual in nature. Finally, in 2016, Adams *et al.* showed that in 16 male and 16 female participants who undertook the 2014 Falmouth road race (11.3km), percentage bodyweight loss ($\leq 2.5\%$) was predictive of faster finishing time ($R^2 = 0.19$; $p = 0.018$), faster average pace ($R^2 = 0.29$; $p = 0.012$) and greater percentage from predicted finish time ($R^2 = 0.15$; $p = 0.033$) (Adams *et al.*, 2016).

Percentage bodyweight losses and performances in the above investigations suggest that exercise induced hypohydration may be beneficial over moderate exercise durations with respect to exercise performance, this may be driven by improvements in exercise economy and mechanical efficiency due to an acute reduction in bodyweight. However, in hot temperatures ($\geq 30^{\circ}\text{C}$) this ‘tactical hypohydration’ is to be discouraged, as bodyweight losses are likely accelerated and so elevations in T_{skin} may increase cardiovascular strain and impair $\% \dot{V}\text{O}_{2\text{max}}$ and \dot{Q} that can be recruited during exercise performance.

2.4.1.6 Respiratory alterations and effects upon substrate oxidation

Perhaps the most familiar mental image when one considers respiration and the heat is that of a panting dog. Panting is considered an evaporative cooling mechanism, and is used to regulate T_{core} within dogs upon exposure to hot temperatures (Anrep and Hammouda, 1932). In humans under heat exposure, this response may be described as thermal hyperpnea, or hyperthermic hyperventilation (M. D. White, 2018) and whilst unlikely to be the primary thermoregulatory mechanism during exercise in hot conditions unless sweating is compromised (M. D. White, 2018). Some cooling via H_{resp} may occur due to an increase in $\dot{V}\text{E}$, as gases’ capacity for retaining moisture increases with temperature (Kenny and Jay, 2013).

Elevated $\dot{V}\text{E}$ serves further useful functions during exercise such as increasing blood pH and decreasing bicarbonate stores (due to increased $[\text{H}^+]$ efflux) and lowering PaCO_2 (Nybo, Rasmussen and Sawka, 2014), proportional to the increase in $\dot{V}\text{E}$ (Tipton *et al.*, 2017), but potentially at the cost of reducing brain blood flow and thus cerebral cooling (Nielsen and Nybo, 2003; Nybo, 2012; Tipton *et al.*, 2017). The mechanism by which $\dot{V}\text{E}$ increases in the heat is thought to be a combination of respiratory frequency and tidal volume, themselves elevated by increased central command and associated metabolites, as well as heat *per se* (Tipton *et al.*, 2017).

Increases in $\dot{V}\text{O}_2$ and thus $\% \dot{V}\text{O}_{2\text{max}}$, are observed in the heat, but are mediated by a range of factors across various physiological systems such as T_{skin} (section 2.4.1.4), sweat rate (section 2.4.1.5) and core (section 2.4.1.3) and brain (section 2.4.1.2) temperatures. As exercise duration increases in the heat $\dot{V}\text{O}_{2\text{max}}$ is lowered (most likely due to a reduction in \dot{Q}), and thus the ability to respond to high intensity exercise demands is diminished (Nybo *et al.*, 2001). These effects are thought to be due to a reduction in $\dot{V}\text{O}_{2\text{max}}$ (most likely due to its multifactorial nature) as opposed to a reduction in $\dot{V}\text{O}_2$ kinetics (Nybo *et al.*, 2001).

Downstream metabolism, i.e. substrate metabolism, is clearly affected by alterations in $\dot{V}O_2$ during exercise in the heat; these effects do not solely respond to alterations in gaseous exchange, but also respond to alterations in the internal milieu of the muscle and potentially muscle temperature (Q_{10} effect). This was first shown by Fink and colleagues in 1975, who demonstrated approximately a two-fold increase in lactate and glycogenolysis, and a halving in the rate of lipolysis in biopsied muscle following 60 min of exercise in hot (41°C) compared to cold (9°C) conditions (Fink, Costill and Van Handel, 1975), which they attributed to a reduction in muscle blood flow. There is also evidence to suggest that exercise in hot conditions may alter adrenal responses to exercise and muscle fibre type recruitment (Febbraio *et al.*, 1994; Febbraio, 2001), which may accelerate fatigue in and of itself, but further emphasises that an increased rate of glycolysis and glycogenolysis is likely a contributory factor to fatigue during exercise in the heat.

These effects may be partially mitigated by the ingestion of exogenous carbohydrate during exercise in the heat (Carter, Jeukendrup and Jones, 2005; Leites *et al.*, 2016), preferably from multiple transportable sources (Jentjens *et al.*, 2006). Note that in the heat it is predominantly neither the availability of carbohydrate, nor increased carbohydrate oxidation that are considered contributory factors to fatigue, both of which have been known to improve performance since the early 20th century (Krogh and Lindhard, 1920; Levine, Gordon and Derick, 1924; B. Gordon *et al.*, 1925; Edwards, Margaria and Dill, 1934) but the origin of the carbohydrate being oxidised (Fink, Costill and Van Handel, 1975; Febbraio *et al.*, 1994; González-Alonso, Calbet and Nielsen, 1999; Febbraio, 2001).

2.4.2 Perceptual effects and responses

The previous subsection outlined physiological effects and responses of exercising in hot environmental conditions. However, attending to perceptual symptoms of heat exposure may lead to thermoregulatory behavioural modifications (Flouris and Schlader, 2015), the first of which is a reduction in exercise intensity (Schlader, S. R. Stannard and Mündel, 2011; Schlader, Simmons, Stannard and Mündel, 2011b). Tending to perceptual factors through either thermal (see section 2.5) or non-thermal interventions (e.g. menthol; section 2.5.1) may improve exercise performance in the heat, but whether this confers a risk to health and homeostasis beyond the exercise bout remains to be elucidated (Stevens and Best, 2017; Best, Payton, *et al.*, 2018) and most likely depends upon the nature and severity of the intervention employed.

2.4.2.1 Thermal Comfort and Thermal Sensation

Behavioural thermoregulation was first examined by Weiss and Laties (1961) and was to ‘specify the relation between body temperature and a response which provided an exteroceptive source of heat’ (Weiss and Laties, 1961). This response can be divided and quantified as sensations representing perceived thermal pleasantness and interoceptive temperature detection. Specifically, thermal comfort is considered the affective component of temperature detection and is an assessment of how satisfactory the thermal environment is to an individual (Bligh and K. G. Johnson, 1973) and may best be described as a perceived thermal ambivalence (Flouris and Schlader, 2015). Whereas thermal sensation can be considered the intensity of temperature perceived by an individual (Attia, 1984). During exercise it appears that thermal sensation and RPE are the primary drivers of behavioural thermoregulation, whereas at rest thermal comfort is the dominant perceptual stimulus (Attia, 1984; Flouris and Schlader, 2015). The strength of this relationship may be determined in part by aerobic fitness (Zora *et al.*, 2017).

Exercise in hot conditions increases thermal sensation, and decreases thermal comfort, but unlike physiological symptoms of heat stress the rate of increase does not appear to be correlated with exercise intensity (Schlader, Simmons, Stannard and Mündel, 2011a), but exercise intensity may be determined by thermal comfort and sensation at the onset of exercise (Schlader, Simmons, Stannard and Mündel, 2011a). A causal role cannot be established however, as alterations in thermal perception are underpinned by changes in physiological systems (Cabanac, 1971; Cheung, 2007; 2010; Schlader, S. R. Stannard and Mündel, 2011) and to a certain extent, vice versa, as modification of exercise intensity itself can be considered a thermoregulatory behaviour.

Thermal comfort and thermal sensation are primarily driven by increases in T_{skin} , until the point of hyperthermia when T_{core} becomes the primary factor in thermal comfort determination, whereas thermal sensation is modified independently of T_{core} (Schlader *et al.*, 2009; Schlader, S. R. Stannard and Mündel, 2011; Schlader, Simmons, Stannard and Mündel, 2011a; Vargas *et al.*, 2018). This is logical as behavioural modifications and heat stimuli can more readily manipulate T_{skin} than T_{core} , also modifications in T_{skin} will likely affect peripheral blood flow and regional sudomotor activities, as outlined in sections 2.4.1.4 and 2.4.1.5, and may be countered via thermal strategies (Schlader, Simmons, Stannard and Mündel, 2011b; Mündel, Raman and Schlader, 2016) which are discussed in section 2.5.

2.4.2.2 Thirst

Thirst is a complex phenomenon with a relatively simple purpose of ensuring hydration within the homeostatic limits. Eccles (2000), notes that thirst can be defined broadly as a sensation of a desire for water; but this fails to differentiate between factors that contribute to thirst such as a general thirst drive, acute mouth dryness or the salt content of foods and beverages (Eccles, 2000). Instead, Eccles recommends Epstein's 1991 definition that thirst is defined as 'the specific, central motivational state of readiness to consume water.' (A. N. Epstein, 1991). Epstein clarifies 'by central of course, I mean it goes on in the brain.' This comment is important for the present thesis, as unlike thermal comfort or sensation it is not driven by peripheral factors such as an increase in T_{skin} or even T_{core} (Cleary, Toy and Lopez, 2014; Armstrong *et al.*, 2015; Armstrong, Johnson, *et al.*, 2016; Funnell *et al.*, 2019), but is instead driven by dedicated neural networks (Gizowski and Bourque, 2017; Augustine *et al.*, 2018; Zimmerman *et al.*, 2019), and supported by osmolality receptors, anti-diuretic hormone and aldosterone (Thornton, 2010), as thirst ultimately is the perceptual representation of blood osmolality and wider body fluid homeostasis (Eccles, 2000; Gizowski and Bourque, 2017).

In hot conditions thirst is typically elevated (Cleary, Toy and Lopez, 2014; Armstrong *et al.*, 2015; Armstrong, Johnson, *et al.*, 2016), and in lab conditions increases proportionally ($p < 0.02$) to percentage bodyweight lost due to exercise in the heat (Engell *et al.*, 1987). If thirst was not tended to through water ingestion and symptoms were to progress to the point of catastrophe, this would naturally accelerate other physiological factors associated with fatigue related to blood; such as blood temperature, rate of perfusion of working musculature and skin, T_{skin} and \dot{Q} , due to an elevated HR and decreased SV.

In ecologically valid conditions, a range of thirst advice is provided, from drinking to thirst (Noakes, 2010) to drinking to a prescriptive schedule (Kenefick, 2018), however factors such as event duration, event intensity, opportunity for drinking, fluid provision on course, personal tolerance and the anticipated ambient temperature during an event must also be considered. Examples of this multi-faceted approach are prevalent in ultra-running literature (Stellingwerff, 2016; Hoffman, Stellingwerff and Costa, 2018; Best, Barwick, *et al.*, 2018), but likely apply to all other sports that employ fluid provision strategies, especially when competing in the heat (Kenefick, 2018). Managing these factors is a challenge, but in most instances, athletes do not have access to information or methods of assessment of some of these variables during competition, and so provided event duration is < 1.5 hours and conditions are not hot (e.g. $> 28^{\circ}\text{C}$) (Kenefick, 2018), drinking may be self-directed on the condition that drinking behaviour does not increase bodyweight, but

bodyweight reductions of ~2-3% may be permissible based upon information presented in section 2.4.1.5.

The temperature of fluids ingested (during exercise) may affect the degree of thirst satiation provided by that beverage (Brunstrom and Macrae, 1997; van Belzen, Postma and Boesveldt, 2017), and cold drinks in hot temperatures have been repeatedly shown to improve endurance performance (Burdon *et al.*, 2010a; Riera *et al.*, 2014; Tran Trong *et al.*, 2015). These responses may be both physiologically and perceptually mediated, as a beverage that is sufficiently cool enough to lower T_{core} during exercise would likely also provide a sensory refreshing stimulus (Eccles *et al.*, 2013). The maintenance of such cold drink temperatures presents an applied problem for practitioners, but is also confounded by thermo-sensory afferents such as menthol (Eccles, 2000) which may also attenuate thirst as a result of stimulation of oral cold receptors (see section 2.5.1).

To conclude thirst in and of itself does not cause fatigue during endurance exercise performance (in hot conditions) but may be an indicator that blood-borne changes in water and sodium content have occurred or are occurring. These changes may have downstream effects that work to limit endurance performance more directly.

2.4.3 Manifestations in performance

Ultimately, exposure to heat during exercise can increase the physiological strain, and perceptual assessment of such strain, placed upon an athlete. These symptoms worsen as exercise increases in duration and intensity. Hence, methods are employed to attenuate physiological and or perceptual symptoms experienced during exercise in the heat; these are typically applied topically or ingested and can be administered before or during exercise, or throughout the entire exercise bout. The next section will briefly introduce these strategies, which are further reviewed and their effects quantified in Chapter 3.

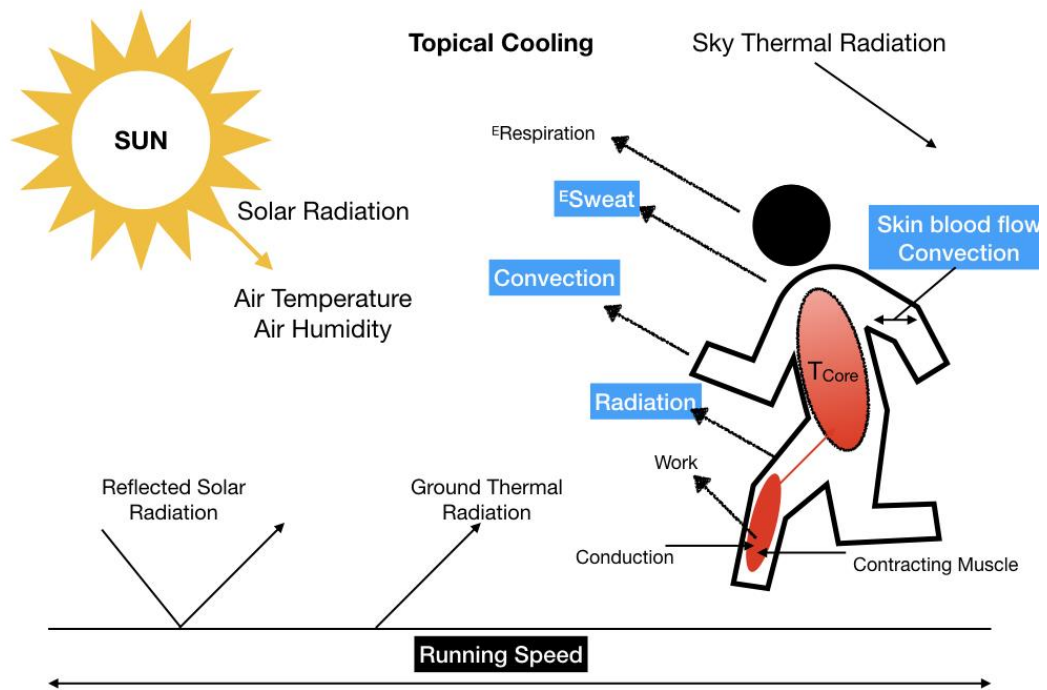
2.5 Methods employed to cool athletes

Athletes performing in hot environments may employ cooling strategies before, during and between exercise bouts to reduce the physiological and perceptual strain experienced, in turn this may improve performance. Chapter 3 provides a systematic review and meta-analysis of topical and oral cooling strategies with respect to time trial performance, so this section aims to briefly introduce these concepts and outline their physiological and performance implications.

Topical cooling strategies (Figure 2) work by either physiologically or perceptually lowering the temperature of the skin by either altering the gradient between the T_{core} and the periphery or between T_{skin} and the environment, or applying a potent cold stimulus to

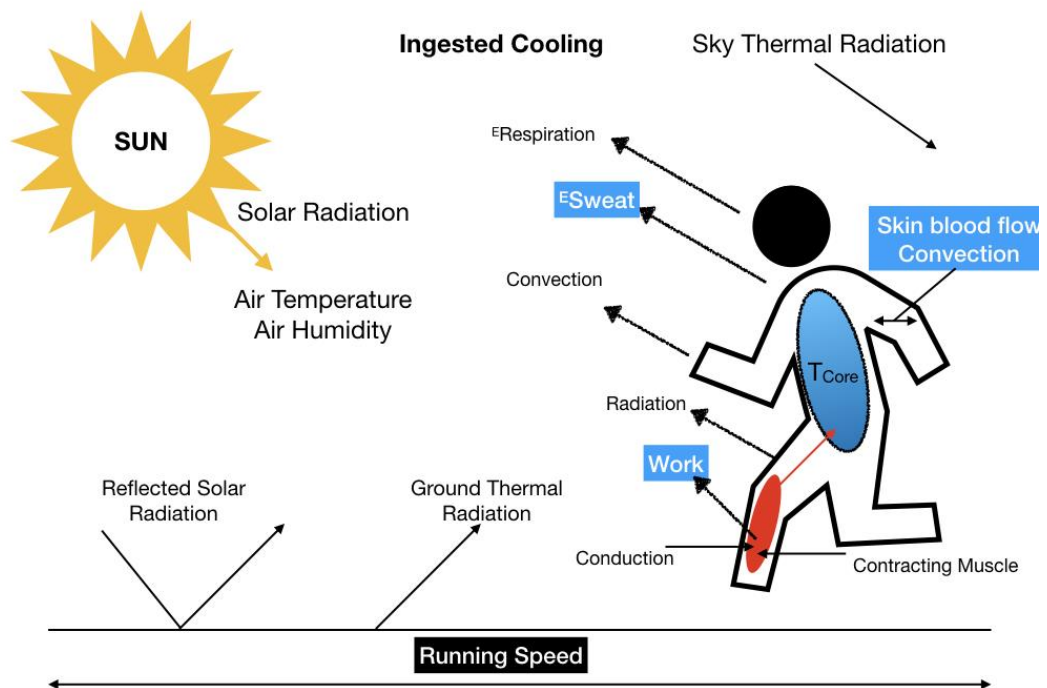
a large cold sensitive area such as the neck, chest or back (Filingeri, 2011). Known effects of topical cooling are alterations in sweat rate and skin blood flow (Gillis, Weston, House and Tipton, 2015), and improvements in perceptual factors (e.g. thermal comfort and or thermal sensation (Kay, Taaffe and Marino, 1999; Arngrimsson *et al.*, 2004; A. B. Stannard *et al.*, 2011; Sheadler *et al.*, 2013; Guéritée *et al.*, 2015; Gillis, Weston, House and Tipton, 2015). Altered rates of heat accumulation during exercise are also noted, but most older literature concerning topical (physiological) cooling is partially flawed due to the impracticality of the methods used to cool athletes such as exposure to cold air of 0-5°C (Cotter *et al.*, 2001), although this acts as a strong mechanistic control in comparison to other topical cooling strategies.

Cold water immersion presents a small advance in this area and has indeed shown performance improvements (Marsh and Sleivert, 1999; Peiffer *et al.*, 2010; Siegel *et al.*, 2011; Rinaldi *et al.*, 2018; Choo *et al.*, 2019) brought about by a reduction in body temperature, but again the reality of athletes participating in this prior to competitive exercise, which has scheduled call room procedures and equipment checks, is speculative. Cooling garments such as ice vests (Cotter *et al.*, 2001; Arngrimsson *et al.*, 2004; Hasegawa *et al.*, 2005; A. B. Stannard *et al.*, 2011; Randall, E. Z. Ross and Maxwell, 2015) or water perfused suits (Cotter *et al.*, 2001; Hsu *et al.*, 2005; Sheadler *et al.*, 2013; Carrasco, 2013) may present a more user friendly method of cooling athletes topically, and are possibly more efficacious as they are applied to large heat sensitive areas, and lower blood and core temperatures (N. F. Gordon, Bogdanffy and J. Wilkinson, 1990; Cotter *et al.*, 2001; Carrasco, 2013), extending exercise performance by the creation of a short term 'heat sink' (N. A. S. Taylor, Tipton and Kenny, 2014).



Adapted from Gisolfi & Wenger, 1984

Figure 2-3 Schematic diagram highlighting the factors targeted by topical cooling methodologies e.g. ice vests, pre-exercise cold water immersion



Adapted from Gisolfi & Wenger, 1984

Figure 2-4 Schematic diagram highlighting the effects of ingested cooling methodologies on heat production, transfer and loss

The notion of a ‘heat sink’ is more evident when athletes undertake ingested cooling, in the form of ice slurries (Siegel *et al.*, 2010; 2011; Stevens *et al.*, 2013) or cold beverages (Mündel *et al.*, 2006; J. K. W. Lee and Shirreffs, 2007; J. K. Lee, Shirreffs and Maughan, 2008; Burdon *et al.*, 2010a; 2010b; Maunder, Laursen and Kilding, 2016). Ingested cooling actively lowers T_{core} and in doing so favourably alters the gradient between T_{core} and T_{skin} (Kenefick *et al.*, 2007), which permits a greater rate of heat accumulation throughout the exercise bout and has been shown to improve cycling and running performance (Siegel *et al.*, 2010; 2011; M. L. Ross *et al.*, 2012; Levels *et al.*, 2013; Stevens *et al.*, 2013; Maunder, Laursen and Kilding, 2016) and time to exhaustion (Siegel *et al.*, 2010).

Recent work has shown that ingesting ice late in the exercise bout may improve cycling time to exhaustion in hot environmental conditions (Jeffries, Goldsmith and Waldron, 2018); here ice serves to reset the thermal interpretation of exercise stress and attenuates the environmental stress received by thermoreceptors. The same study also showed non-thermal cooling, achieved by menthol mouth swilling, to be effective (Jeffries, Goldsmith and Waldron, 2018). Menthol and ice share the same molecular target, and have demonstrated improvements in time trial performance in tropical environments when co-ingested (Riera *et al.*, 2014; Tran Trong *et al.*, 2015). Menthol has also shown promise as a non-physiological topical cooling strategy; the following section will explore the mechanism underpinning menthol’s ability to impart perceptual sensations of cool, and improve exercise performance when applied topically or orally.

2.5.1 Menthol as a novel cooling strategy during exercise

The effects of menthol have long been known to impart feelings of cool and freshness. Menthol was characterised by German chemist F.L. Alphonse Oppenheim, first in French in 1861 (Oppenheim, 1861) and again in English in 1862 (Oppenheim, 1862), as the camphor of mint; as it is analogous to camphoric alcohol the name menthol is aptly derived from *Mentha piperita*, the Latin for peppermint. Academic literature dating to 1890 espouses the benefits of menthol for respiratory infections (Potter, 1890) and cooling via stimulation of thermoreceptors is first noted in 1896 (Somers, 1986). The first documented case of menthol poisoning also notes a cooling sensation from the blood (Schwenkenbecher 1906 in (Hensel and Zotterman, 1951). These subjective abilities of menthol to alleviate nasal congestion and impart sensations of cooling are excellently reviewed by Ronald Eccles, who has written a number of summaries pertaining to menthol’s cooling characteristics and associated psychophysiological responses that form the backbone of this thesis (Eccles, 1994; 2000; Eccles *et al.*, 2013).

Recently, menthol has been adopted as a cooling strategy to attenuate perceptual symptoms associated with exercising in the heat such as thermal comfort and sensation. Typically, menthol is applied before and or during exercise, with oral and topical administration of menthol targeting differing perceptual and thermoregulatory mechanisms. These are introduced here, with a systematic review of the literature presented in Chapter 4, before subsequent investigation throughout the remainder of the thesis.

Menthol is administered in two forms with respect to the exercise bout. Topically, menthol may be applied as a cream/gel (Kounalakis *et al.*, 2010; Topp *et al.*, 2011; Akehi and Long, 2013; Topp, Ledford and Jacks, 2013; Valente *et al.*, 2015; Botonis *et al.*, 2016) or as a spray (Gillis, House and Tipton, 2010; Barwood, Corbett and D. K. White, 2014; Gillis, Weston, House and Tipton, 2015; Barwood, Kupusarevic and Goodall, 2018a); these products may contain complimentary ingredients or surfactants with a view to increasing product efficacy, marketability or ease of application. Menthol containing topical products are often used to treat pain, as menthol can act as an analgesic and counterirritant (Galeotti *et al.*, 2002; Gaudioso *et al.*, 2012), but concentrations >30% menthol may elicit pain (Gaudioso *et al.*, 2012). Menthol can also be administered orally, as a mouth swill (Mündel and D. A. Jones, 2009; Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016; Flood, Waldron and Jeffries, 2017; O. R. Gibson, Wrightson and Hayes, 2018; Jeffries, Goldsmith and Waldron, 2018) or co-ingested with other physiological cooling strategies (Riera *et al.*, 2014; Tran Trong *et al.*, 2015; Riera *et al.*, 2016); these strategies expose menthol to cold sensitive nerve endings of the mandibular and maxillary branches of the trigeminal nerve (Hummel and Livermore, 2002; Lu *et al.*, 2013).

Both strategies elicit sensations of cooling and do so by stimulating transient receptor potential melastatin 8 (TRPM8) receptors. These are voltage gated ion channels embedded within cell membranes and are especially prevalent in the dorsal and trigeminal ganglia (Kalantzis, Robinson and Loescher, 2007; Nazıroğlu and Özgül, 2011) but are also found in the upper gut, vascular smooth musculature, bladder and male genitalia (Nilius and Owsianik, 2011). Upon stimulation, through either a fall in temperature to below 26°C or application of menthol or eucalyptol, there is a depolarisation and the electric potential of the membrane is altered due to a flux in Ca²⁺ and Na⁺ ions, and subsequent generation of an action potential (Galeotti *et al.*, 2002; Gaudioso *et al.*, 2012). If a menthol containing stimulus is applied at a sufficient concentration/intensity, either orally or topically, behavioural, physiological and sensation modifications may occur. This has been shown elegantly by Bautista and colleagues (2007), who demonstrated that if the genes for

TRPM8 were ‘knocked out’ in mice there was a loss of cold and menthol sensitivity down to a temperature of 10°C (Bautista *et al.*, 2007) and in doing so highlight TRMP8’s role as the primary detector of environmental cold. It is also noteworthy that menthol stimulates in a manner that is inversely proportional to the thickness of the stratum corneum in the area on which it is applied (H. R. Watson *et al.*, 1978). This explains the use of the tongue as a tissue of interest in most animal research concerning the absorption and resultant excitation of nerve fibres following menthol application, and the less potent effects observed when menthol is applied topically during exercise.

Topical application of menthol prior to or during exercise has consistently been shown to ameliorate subjective thermal sensations during endurance exercise (Barwood *et al.*, 2012; Barwood, Corbett and D. K. White, 2014; Barwood *et al.*, 2015; Gillis, Weston, House and Tipton, 2015; Gillis *et al.*, 2016; Barwood, Kupusarevic and Goodall, 2018b), but increases in sweat rate, skin blood flow and heat storage (Gillis *et al.*, 2016) have also been shown, as per Figure 2.4. This may or may not (positively) influence exercise performance, and likely depends upon the strength (i.e. concentration or area to which menthol is applied) or frequency of the ‘signal’ brought about by menthol application. This has recently been exemplified by Barwood and colleagues (Barwood, Kupusarevic and Goodall, 2018) who showed that a repeated application of menthol, delivered via a spray at 0.20% menthol at 20 and 40 min of an exercise bout consisting of 45min fixed work and a TTE (70% maximum power), improved TTE. This had previously not been shown following single application by the same research group, in similarly designed studies (Barwood *et al.*, 2012; Barwood, Corbett and White, 2014; Barwood *et al.*, 2015), suggesting a relatively quick decay in menthol’s effects that may be mediated by exercise intensity and the rate of evaporative cooling, driven by the exercise environment e.g. wind-speed; these effects are also known to be exaggerated if a topical application contains alcohol (Gillis *et al.*, 2016).

Menthol may also be applied topically as an analgesic, or more purposefully through resistance exercise (Gillis *et al.*, 2018). These methods elicit similar sensations to those described above, and demonstrate ergogenic effects when applied repeatedly in response to an exercise stimulus too. Menthol application (4% cream) has been shown to facilitate muscular recovery (quantified via vertical jump performance; +1-5cm in comparison to placebo or control cream) following exercise induced muscle damage (Gillis *et al.*, 2018), with authors unsure as to whether menthol accelerates recovery through enhanced tissue capabilities, motivational factors, motor unit recruitment, or factors not otherwise stated (Gillis *et al.*, 2018). Further topical research is outlined in Chapter 4, but with respect to

endurance exercise it appears that unless menthol application is repeated and applied to a sufficiently thermosensitive area it is unlikely to be ergogenic. With menthol use following exercise that elicits muscle damage, worthwhile improvements in power production can occur, but the mechanism by which this is achieved may be contested.

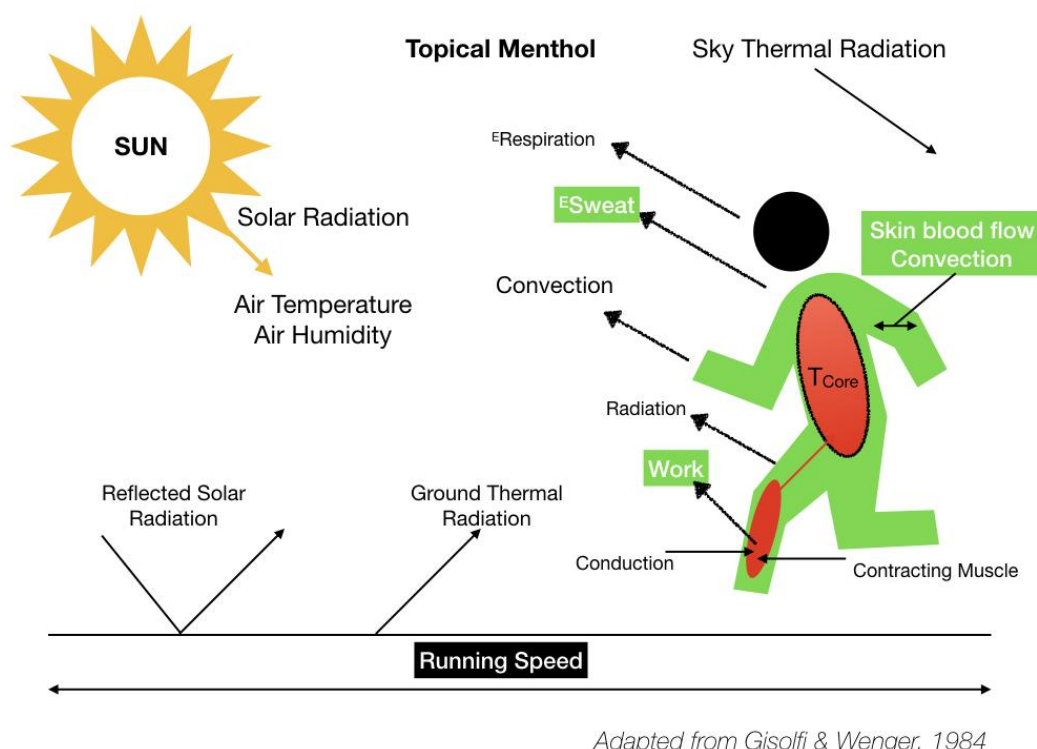


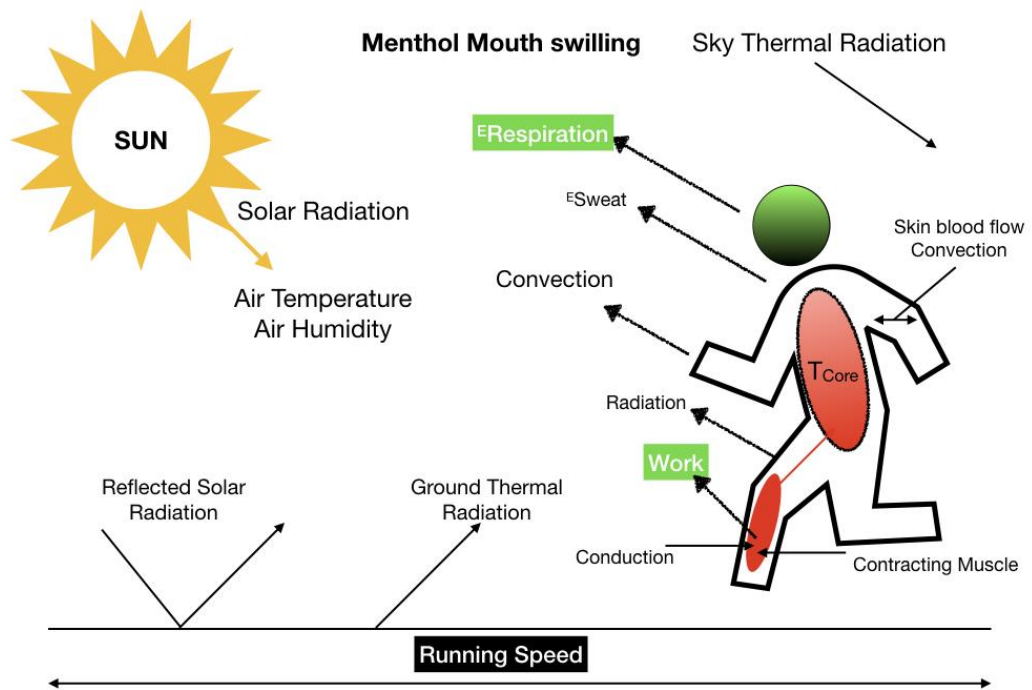
Figure 2-5 The effects of topical menthol application on factors related to temperature regulation. Note that topical menthol application (shown as a green body) may affect green highlighted factors, and may cause an elevation in T_{Core} but an overall increase in work may be observed and manifest in performance enhancement.

Oral application of menthol as a mouth swill or co-ingested with physiological cooling strategies has been consistently shown to lower thermal sensation (Green, 1985; Schlader, S. R. Stannard and Mündel, 2011; Stevens, Thoseby, *et al.*, 2016; Flood, Waldron and Jeffries, 2017; Jeffries, Goldsmith and Waldron, 2018), improve thermal comfort (O. R. Gibson, Wrightson and Hayes, 2018) and increase ventilation (Mündel and D. A. Jones, 2009; Stevens, Bennett, *et al.*, 2016). These effects are depicted in Figure 2.6, and may improve endurance performance either by improving TTE (Mündel and D. A. Jones, 2009; Flood, Waldron and Jeffries, 2017; Jeffries, Goldsmith and Waldron, 2018) or time trial performance (Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016); these effects have not been observed when oral menthol administration takes place during intermittent exercise (O. R. Gibson, Wrightson and Hayes, 2018), and interestingly are also not seen when menthol's sensory counterpart capsaicin is swilled (O. R. Gibson, Wrightson and Hayes, 2018), although (commercial) reports of cramp prevention are made (Murray,

2017; Craighead *et al.*, 2017). There are no known negative side-effects reported following menthol swilling, nor has oral menthol administration been shown to be ergolytic, but there are points of contention within the literature to date:

Swills used in research have a range of dilution methodologies, and despite most studies employing the same concentration of menthol within the swill inconsistent dilution procedures likely mean that there are between participant differences in the concentration and qualitative characteristics of the swill they are receiving. At the chemical level this issue is evident as menthol is a natural alcohol and thus insoluble in water. Hence the need for investigation into the development of a swill that ensures a thorough and consistent dilution of menthol, at a known concentration. This may have advantages from a commercial point of view with respect to shelf life and the use of known quantities of ingredients, but also to sports nutrition practitioners who can arrange batch-testing of products for anti-doping purposes and more accurately monitor athletes' responses to administration of different menthol concentrations, safe in the knowledge that concentration is the only factor being manipulated.

Further, research to date has administered exercise tests that capture a limited range of exercise intensities and practices (i.e. session designs) with a preponderance of time to exhaustion papers, and supporting time trial performances. Cycling is typically studied due to the experimental control and ease of monitoring (e.g. power production as W). Whilst commendable efforts have been made to assess runners too (Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016), the athletes in these investigations are only moderately trained and so transfer of findings to elite athletes is limited. A final consideration may be the capture of wider qualitative experiences of ergogenic strategy use, especially given that users of supplementation are more likely to respond to a placebo (Hurst *et al.*, 2017a) and that athletes with strong beliefs in supplementation are more likely to respond following its administration (Beedie and Foad, 2009).



Adapted from Gisolfi & Wenger, 1984

Figure 2-6 Schematic diagram highlighting the effects of menthol mouth swilling pertinent to temperature regulation

CHAPTER 3 : TOPICAL AND INGESTED COOLING METHODOLOGIES FOR ENDURANCE EXERCISE PERFORMANCE IN THE HEAT¹

This systematic review and meta-analysis aimed to assess studies which have investigated cooling methodologies, their timing and effects, on endurance exercise performance in trained athletes (Category 3; $\text{VO}_{2\text{max}} \geq 55 \text{ mL} \cdot \text{kg} \cdot \text{min}^{-1}$) in hot environmental conditions ($\geq 28^\circ\text{C}$). Meta-analyses were performed to quantify the effects of timings and methods of application, with a narrative review of the evidence also provided. A computer-assisted database search was performed for articles investigating the effects of cooling on endurance performance and accompanying physiological and perceptual responses. A total of 4129 results were screened by title, abstract, and full text, resulting in 10 articles being included for subsequent analyses. A total of 101 participants and 310 observations from 10 studies measuring the effects of differing cooling strategies on endurance exercise performance and accompanying physiological and perceptual responses were included. With respect to time trial performance, cooling was shown to result in small beneficial effects when applied before and throughout the exercise bout (Effect Size: -0.44 ; -0.69 to -0.18), especially when ingested (-0.39 ; -0.60 to -0.18). Current evidence suggests that whilst other strategies ameliorate physiological or perceptual responses throughout endurance exercise in hot conditions, ingesting cooling aids before and during exercise provides a small benefit, which is of practical significance to athletes' time trial performance.

3.1 Introduction

Heat exposure imposes perceptual and physiological demands on athletes that can be attenuated by interventions; however, the precise timing and best method of administration for these remain unclear. Cooling strategies applied before (precooling) and during (percooling) exercise have been shown to ameliorate deleterious symptoms experienced whilst exercising in the heat (Bongers *et al.*, 2014). Strategies to attenuate these factors are of importance given the increasingly global nature of elite endurance sports, and the

¹ The work presented in this chapter has been accepted for publication in Sports doi: 10.3390/sports6010011

consequent scheduling demands placed upon athletes who often arrive at events with little time for heat-acclimatisation.

Independent of the attenuation of physiological symptoms (Mündel and D. A. Jones, 2009; Cheung, 2010; Castle *et al.*, 2012) improving perceptual symptoms of heat exposure (e.g. thermal comfort and strain) has been shown to improve exercise and cognitive performance (Schulze *et al.*, 2015; Schmit *et al.*, 2017). Recently, subjective measures of athlete wellbeing / fatigue have been shown to be more reliable and sensitive than objective indices in predicting performance, better reflecting acute and chronic training stresses (Saw, Main and Gastin, 2016). These findings highlight the importance of how an athlete feels in determining performance outcomes. This is likely due to an improved 'interoceptive state' (A.D. Craig, 2003) whereby athletes' physiological condition, motivation (A.D. Craig, 2003; Pageaux, 2014) and perception of effort (Swart *et al.*, 2012) are positively affected due to sensations that are perceived to be beneficial in maintaining homeostasis or facilitating task completion (A.D. Craig, 2003; Swart *et al.*, 2012). Hence cooling methodologies which display no physiological effect but improve psychological condition, may still be of value to the athlete with respect to performance.

The emergence of contemporary precooling and percooling strategies, such as ice slurry and menthol mouth swilling, and ice slush ingestion ((Mündel and D. A. Jones, 2009; Riera *et al.*, 2014; Schulze *et al.*, 2015; Tran Trong *et al.*, 2015; Stevens, Thoseby, *et al.*, 2016) have shown improvements in endurance capacity and performance, whilst also being highly practical (Siegel and Laursen, 2012). These strategies may be of most use in elite endurance athletes (Marino, 2002; Wegmann *et al.*, 2012; Schulze *et al.*, 2015) who face extended periods of heat exposure, often on successive days. Therefore, a meta-analysis was conducted to assess the evidence for the performance effects of practical precooling and percooling strategies on well-trained endurance athletes, exercising in the heat. A meta-analysis permitted exploration and quantification of the magnitude of effect different cooling strategies and timings have upon physiological and perceived outcomes which pertain to endurance performance.

3.2 Materials and Methods

Articles investigating ingested and topical precooling and percooling strategies or a combination of both methodologies, were sourced from six online databases (BioMed Central, CINAHL, PlosOne, PubMed, SportDiscus and Web of Science). Reference lists of selected articles were also checked for relevant articles. Where full texts were not available from the University's library, copies were requested from the British Library.

Four search terms were constructed by combining one of four independent variable search terms with a dependent variable term, using the Boolean operator AND. Each search term was performed in each database. The independent variable terms were as follows: Precooling OR pre-cooling OR “pre cooling” OR cooling; Cooling AND Exercise; “Cooling during Exercise”; Cooling AND “during Exercise”. The dependent variable term read: "Time Trial" OR "Time to Exhaustion" OR Power Output OR "Rating of Perceived Exertion".

Included results were limited to full text journal articles written in English, published prior to 11 May 2017. Article titles and abstracts of search results were screened in accordance with exclusion criteria; full texts of the remaining articles were obtained and screened. Within- or between-subjects, repeated measures crossover and randomised controlled trial designs in healthy adults (male only or male and female participants, absent of spinal cord injury, within Performance Level 3 or better ((De Pauw and Roelands, 2013); pooled $VO_{2max} \geq 55 \text{ ml.kg.min}^{-1}$)) conducted in temperatures $\geq 28^{\circ}\text{C}$ were considered for inclusion. Ingested (cold water, ice slurry, menthol) and topical (cooling garments, ice packs, sprays) precooling, percooling and combined (precooling and percooling) methodologies were assessed. Only individual, non-ultra-endurance exercise modalities were considered (Cycling, running, swimming and triathlon completed within the confines of standardised competitive distances or training for such events). Outcome measures had to relate to aerobic exercise performance, with perceptual or physiological measures of heat also being reported. Studies were included on the condition that two reviewers (RB and SP) agreed they met the inclusion criteria. If there was disagreement between reviewers, then a third reviewer (NB) was consulted.

The initial series of searches yielded 4129 results; after screening titles, abstracts and repeats, 43 full texts were obtained. These texts were reduced to 16 in accordance with the inclusion and exclusion criteria, which were then reduced to 11 upon further review (*Figure 3.1*). Data were obtained from authors prior to meta-analysis. Means and Standard Deviations from each study were calculated and used to quantify effect sizes (ES) with accompanying 90% confidence intervals (CI) using specialist software (Review Manager Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.) ES are described as follows: Trivial: 0.0 - 0.2 Small: 0.2 – 0.6 Moderate: 0.6 – 1.2 Large: 1.2 – 2.0 Very Large: 2.0 – 4.0 and Extremely Large: ≥ 4.0 (Hopkins, Marshall, Batterham and Hanin, 2009).

Table 3-1 Details of studies included for meta-analysis including participant number, timings, methods of cooling, exercise modality and study outcomes.

Author	Participants	Timing	Intervention	Modality	Outcomes
Ross et al., 2011	11	Precooling	Ice	Cycling	TT, PO, T _{rec} , TC
Ross et al., 2012	12	Precooling	Ice + T, Ice + G + T	Cycling	TT, PO, RPE, TC
Muñoz et al., 2012	10	Percooling	OR, EXC, EXC + OR	Running	TT, T _{rec} , TC, RPE
Stanley et al., 2010	10	Percooling	Ice, COOL	Cycling	TT, PO, T _{rec}
Stevens et al., 2013	9	Percooling	Ice	Triathlon/Running	TT, T _{rec} , RPE, TC
Stevens et al., 2015	11	Precooling / Percooling	Ice, M	Running	TT, T _{rec} , RPE, TS
Stevens et al., 2017	9	Percooling	M	Running	TT, T _{rec} , RPE, TS
Riera et al., 2014	12	Combined	N, N + M, COOL, COOL + M, Ice, Ice + M	Cycling	TT, TC, TS, RPE
Tran Trong et al., 2015	10	Combined	N + M, COOL + M, Ice + M	Cycling/Running	TT, TC, TS, RPE
Schulze et al., 2015	7	Combined	Ice, PC + Ice	Cycling	TT, PO, T _{rec} , TC, TS

Intervention Methodologies: COOL: cool liquid ingestion; EXC: external cooling via pouring cold water; G: glycerine; Ice: ice slurry ingestion; N: ambient temperature water; M: menthol; OR: oral rehydration; T: iced towels applied to participants. Outcome Variables: TT: time trial performance; PO: power output; RPE: rating of perceived exertion; T_{rec}: rectal temperature; TC: thermal comfort; TS: thermal sensation.

Methodologies employed, as well as perceptual and physiological outcomes for each study are detailed in Table 3.1. Methodological quality of studies was assessed using the previously validated PEDro Scale (de Morton, 2009). A publication bias is acknowledged given the trained nature of the participants studied and the emphasis placed upon the practicality of the strategies under review.

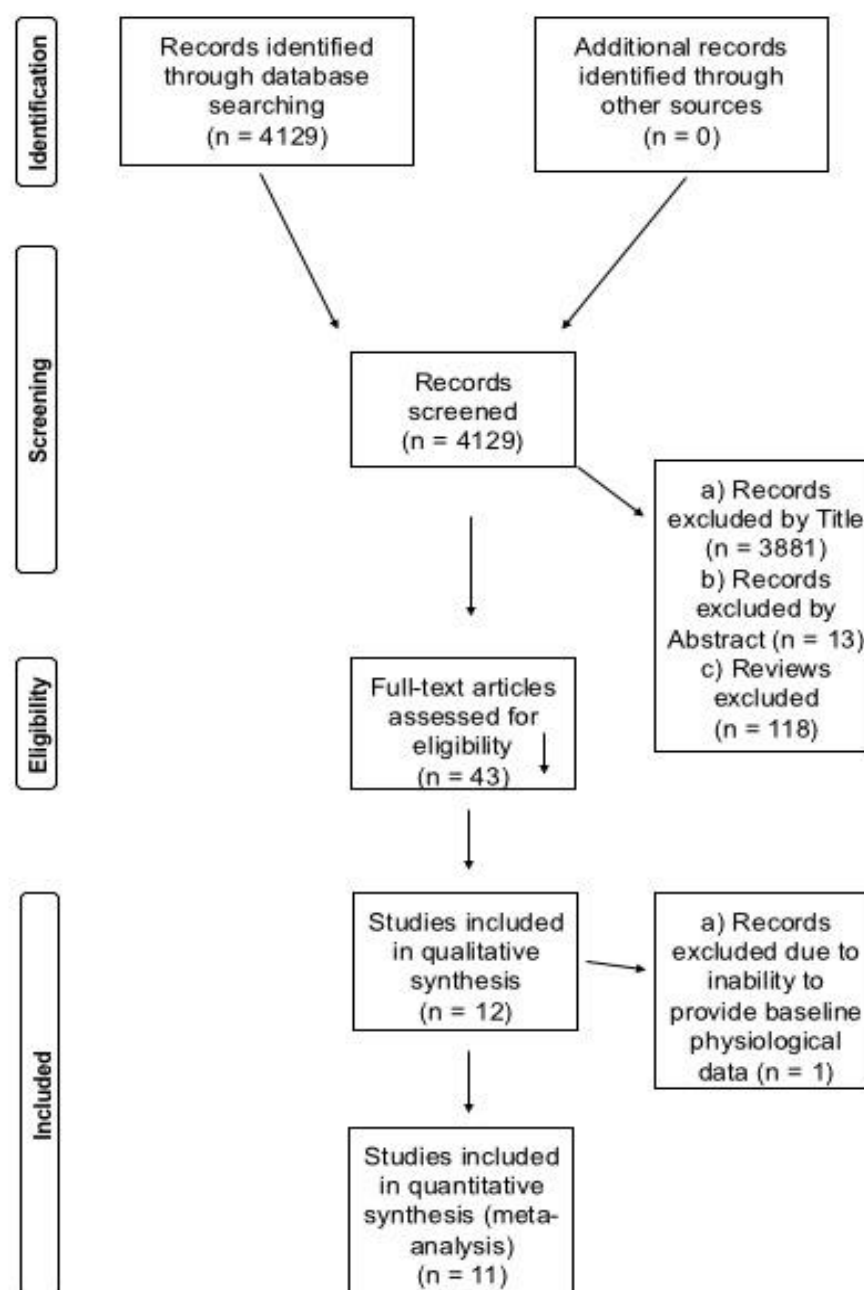


Figure 3-1 Flow chart to depict the study search, screening, and inclusion process.

3.3 Results

3.3.1 General Findings

Eleven studies, with a combined sample of 101 athletes (310 observations), were included for meta-analysis; participants had a pooled $\text{VO}_{2\text{max}}$ of $63.09 \pm 4.55 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$. Of the 10 studies included for meta-analysis 3 employed precooling, 5 percooling, and 3 combined intervention timings; with 5 utilising topical, 7 ingested, and 3 combined cooling methodologies. PEDro Scoring revealed all studies to be of high quality (PEDro Score 6). We observed non-significant, low heterogeneity ($Q = 11.06$, ($p = 0.92$), $I^2 = 0\%$) across all studies. Raw differences (Δ performance; seconds) in time trial performances are presented in Table 3.2

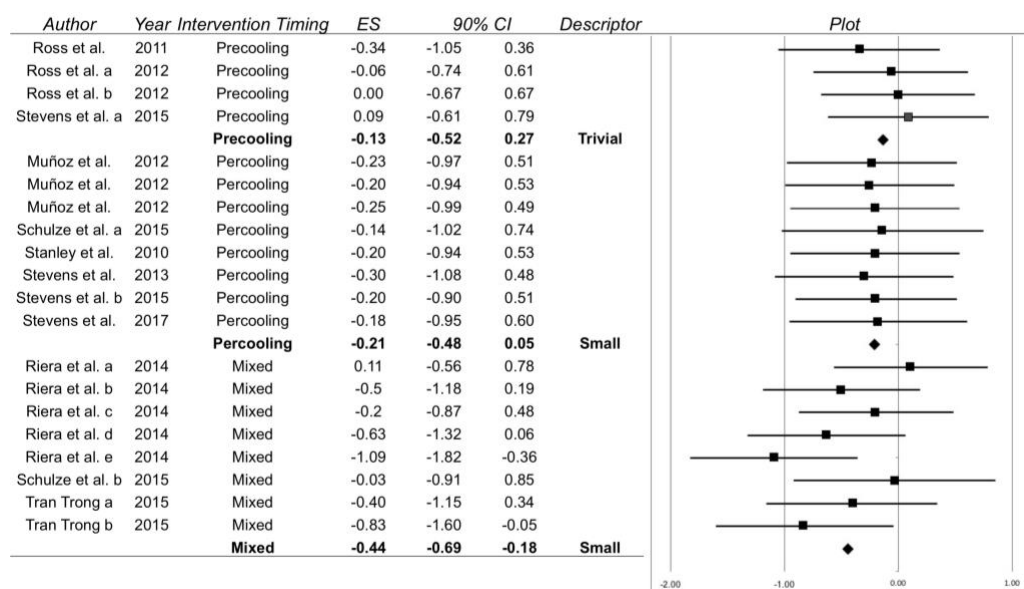
Table 3-2 Change in time trial performance of studies included for meta-analysis including timings and methods of cooling.

Author	Timing	Intervention	Δ Performance (s)
Ross et al., 2011	Precooling	Ice	-66.0 ± 29.4
Ross et al., 2012	Precooling	Ice + T	-18.6 ± 28.8
-	-	Ice + G + T	0.0 ± 1.2
Muñoz et al., 2012	Percooling	OR	-60.0 ± 81.0
-	-	EXC	-48.0 ± 85.2
-	-	EXC + OR	-63.0 ± 52.2
Stanley et al., 2010	Percooling	Ice	-33.6 ± 60
Stevens et al., 2013	Percooling	Ice	-72.0 ± 18.0
Stevens et al., 2015	Precooling	Ice	18.0 ± 12.0
-	Percooling	M	-42.0 ± 6.0
Stevens et al., 2017	Percooling	M	-36.0 ± 6.0
Riera et al., 2014	Combined	N + M	-49.8 ± 33.6
-	-	COOL	36 ± 139.8
-	-	COOL+M	-162.6 ± 39.0
-	-	Ice	-121.2 ± 12.6
-	-	Ice + M	-232.8 ± 51.0
Tran Trong et al., 2015	Combined	COOL+M	-136.2 ± 252.0
-	-	Ice + M	-283.2 ± 232.8
Schulze et al., 2015	Combined	Ice	-23.4 ± 0.0
-	-	Ice + T	4.8 ± 6.0

Intervention Methodologies: COOL: cool liquid ingestion; EXC: external cooling via pouring cold water; G: glycerine; Ice: ice slurry ingestion; N: ambient temperature water; M: menthol; OR: oral rehydration; SC: scalp cooling; T: iced towels applied to participants.

3.3.2 Timing of Cooling Methods

Mixed timings (a combination of precooling and percooling) were found to be the most effective timing with respect to time trial performance (Effect Size = -0.44; 90% Confidence Interval -0.69 to -0.18), with pre and percooling demonstrating trivial and small effects respectively. Power output was trivially improved by precooling (0.17; -0.18 to 0.52) and percooling (0.16; -0.40 to 0.73), with no power output data reported for mixed timings. Percooling (-0.37; -0.65 to -0.10) and precooling (-0.42; -0.93 to 0.10) strategies demonstrated small reductions in rectal temperature, whereas precooling elicited a near moderate decrease (-0.59; -0.90 to 0.28). Effects upon perceptual measures were varied. Thermal comfort and sensation were found to be most receptive to percooling (1.29; -0.82 to 1.76 and -0.60; -1.51 to 0.31 respectively). Small beneficial reductions in RPE were found following percooling (-0.39; -0.70 to -0.08) and mixed (-0.48; -0.75 to -0.22) timings, whereas precooling trivially influenced RPE (0.17; -0.18 to 0.52).



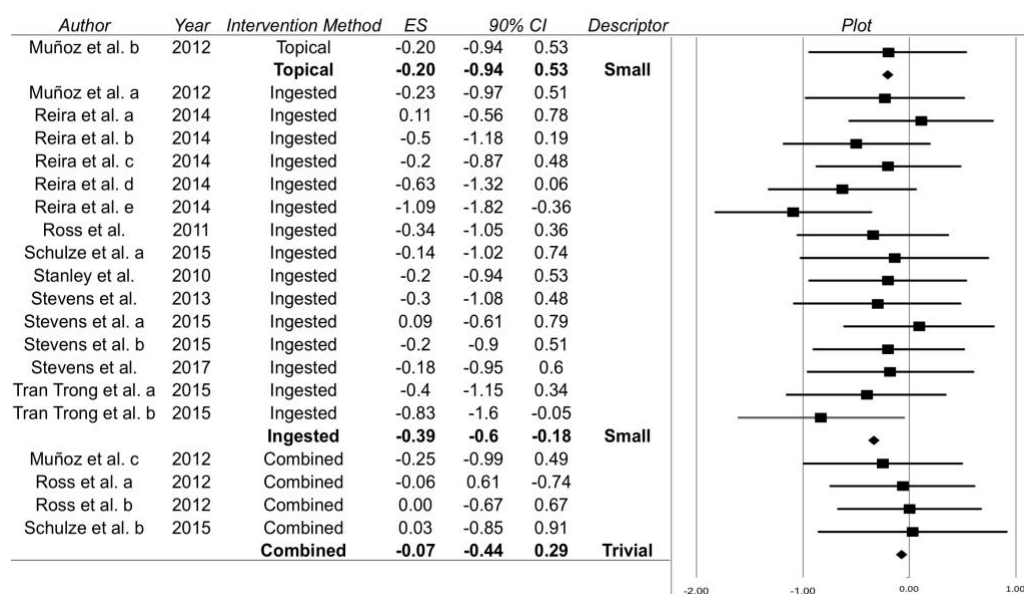


Figure 3-2 Forrest plot displaying the difference in time trial performance between the experimental group and control group for each individual case; (a) when employing differing cooling strategies and (b) when administering strategies at different time points. ES: Effect Size; ■: Mean response for an individual study; ♦: Pooled effect size for included studies.

3.3.2 Application of Cooling Methods

Small improvements in time trial performance (-0.33; -0.52 to -0.14) and power output (0.22; -0.22 to 0.66) were seen following ingested cooling methodologies. Similarly, small effects were also observed in topical (-0.20; -0.94 to 0.53 and 0.34; -0.40 to 1.08, time trial performance and power output respectively) strategies, yet combined strategies showed trivial effects (-0.07; -0.44 to 0.29 and 0.02; -0.39 to 0.44, as above). Rectal temperature was most sensitive to ingested (-0.47; -0.68 to -0.26) methodologies presenting moderate effects. This was not supported by measures of thermal comfort for which large reductions were found following application of topical strategies (-1.35; -2.18 to -0.51); Thermal sensation was most sensitive to combined strategies (-0.36; -1.25 to 0.53). Topical (-0.50; -1.03 to 0.04) and ingested (-0.41; -0.61 to -0.20) methodologies induced small beneficial effects upon RPE with trivial effects found when combined strategies were applied (-0.13; -0.53 to 0.27).

3.4 Discussion

This meta-analysis aimed to assess the effects of practical precooling and percooling strategies applied to trained endurance athletes exercising in hot environmental conditions. Our main finding was that combining precooling and percooling timings has a cumulative beneficial effect upon endurance time trial performance, compared to when precooling and percooling are implemented in isolation (Figure 3.2a). Our secondary finding was that

ingested cooling methods outperform topical, or a combination of methods, suggesting method of delivery affects the performance enhancing capabilities of cooling interventions (Figure 3.2b). Therefore, when competing in the heat, we recommend ingesting cold liquids or ice slurries before and during competition.

This contrasts the conclusions of recent analyses that have suggested precooling and percooling impart similar performance benefits (Bongers *et al.*, 2014), and that combined or topical cooling methodologies are of most value to the athlete (Ross *et al.*, 2013). Mixed timings show a greater effect in the reviewed studies (Figure 3.2a) than when precooling and percooling are performed independently, whereas Bongers *et al.* (2014) found similar effects between precooling and percooling (0.44 and 0.40, respectively). Bongers *et al.* (2014) state an absence of combined cooling timing research (mixed timings) but suggest that implementation of such strategies may prove effective. Our analysis clearly supports their suggestions. This may be a dose response relationship, as combined timings typically include a greater number of cooling exposures than when precooling or percooling is conducted in isolation. The timing of cooling exposures may also have physiological or practical implications, for example, possible interference with warm-up or call room procedures; it may be prudent for event organisers to maximise cooling opportunities in thermally challenging events. This may improve athletes' performances, preserve athlete health (Cheung, Lee and Oksa, 2016), and reduce the prevalence of heat associated illnesses during such events (Racinais *et al.*, 2015).

The clear difference in findings between our and other reviews may also be attributed to a difference in what authors consider 'performance'. We chose to review the effects of cooling on time trial performance, as this is a meaningful measure for endurance athletes. Other reviews (Tyler, Sunderland and Cheung, 2013; Bongers *et al.*, 2014) have grouped endurance outcomes (time trial performance, distance completed, time to exhaustion, power output, etc.) under a broad definition of performance. Whilst cooling may produce similar effect statistics on differing endurance parameters, the tests implemented assess differing endurance functions (capacity vs. performance) (Stevens and Dascombe, 2015) and, importantly, display differing levels of repeatability (Hopkins, Schabort and Hawley, 2001; Stevens and Dascombe, 2015). Similarly, failure to differentiate between cooling methodologies may cloud our understanding of the mechanisms driving performance enhancement. Such differentiation (Ross *et al.*, 2013) may be of use in future studies that plan to tease out the differences between combined methodologies, and for practitioners who require variety in cooling strategies dependent upon athletes' competitive environments and regulations.

Of the chosen methods, combining cooling timings demonstrated the greatest effect on rectal temperature (Small: -0.59 ; -0.90 to 0.28); however, the breadth of confidence interval suggests variability in the rate at which lowering of rectal temperature (Siegel *et al.*, 2010) takes place, and subsequent accumulation of heat (Siegel *et al.*, 2010; Bogerd *et al.*, 2010; Stevens and Best, 2017) across the exercise duration. This variability likely occurs at an individual level, as all included trials were carried out in conditions exceeding the temperature at which metabolic heat production outweighs thermal transfer (Kenny and Jay, 2013). The intensity of precooling (Bogerd *et al.*, 2010) and the subsequent rate of increase in rectal temperature following precooling (Siegel *et al.*, 2010; Bogerd *et al.*, 2010) may contribute to the efficacy of precooling strategies.

It is important to note that the ice slurries used in the majority of included precooling studies contained carbohydrate (Stanley, Leveritt and Peake, 2010; Ross, Garvican and Jeacocke, 2011; Ross *et al.*, 2012; Stevens *et al.*, 2013; 2016), which may have conveyed a physiological advantage beyond precooling alone, although it is acknowledged that the main purpose of carbohydrate in these beverages was to act as an antifreeze (Siegel *et al.*, 2011; Siegel and Laursen, 2012). The amounts of carbohydrate ingested in each study are in congruence with current recommendations for exercise lasting up to 2 hours (≤ 120 g) (Jeukendrup, 2014) and so may have elicited ergogenic effects in these investigations.

Percooling provided a small beneficial improvement in time trial performance (-0.21 ; -0.48 to 0.05), with all studies reporting a mean reduction in time trial performance, despite the use of ingested and topical methods (Stanley, Leveritt and Peake, 2010; Muñoz *et al.*, 2012; Stevens *et al.*, 2013; Schulze *et al.*, 2015; Stevens *et al.*, 2016; 2017). Differences in cooling methodology (ingested; topical) may evoke distinct responses, attributable to differing underpinning mechanisms, despite achieving a uniform effect upon time trial performance when applied throughout the exercise bout. Ingested percooling methods may initially impart perceptual feelings of freshness through stimulation of the cold and menthol sensitive TRPM8 receptors (Patel, Ishiuchi and Yosipovitch, 2007; Schepers and Ringkamp, 2010). Strategies containing menthol improved time trial performance to a greater extent than non-menthol containing counterparts in a temperature dependent manner (Riera *et al.*, 2014; Tran Trong *et al.*, 2015). Menthol has also demonstrated improvements in time trial performance and time to exhaustion when used as a mouth rinse (Mündel and Jones, 2009; Stevens *et al.*, 2016), suggesting that the refreshing sensation or perceptual cooling experienced by an athlete may further enhance the wider physiological effects observed in other percooling studies, especially when isolated to the oral cavity (Stevens and Best, 2017).

Ingested cooling strategies may also act as a thermal buffer, attenuating a rise in rectal temperature, whereby gastrointestinal temperature is reduced prior to exercise commencing (heat sink; Siegel and Laursen, 2012; Riera *et al.*, 2014). Furthermore, it is hypothesised that ice ingestion may cause a mismatch between core and brain temperatures, where the brain perceives the lower local temperature as a greater heat sink than that which has been induced at the core (Siegel and Laursen, 2012; Laursen, 2016). Greater metabolic heat production is then permitted due to this perceived difference, evidenced by the ‘overshoot’ in rectal temperature seen at exercise termination in some ice ingestion studies (Siegel *et al.*, 2010; 2011). Percooling, on the other hand, may permit an initial beneficial rise in core temperature and resultant physiological responses prior to a subsequent dampening of any potentially limiting effects. Percooling may also alleviate subjective thermal measures over a more prolonged duration compared to precooling because of repeated exposures to cold stimuli. This cannot be confirmed by the included studies due to the difference in time trial durations between precooling and percooling conditions. Ingested cooling strategies consumed across the entire exercise window therefore strike a balance between attenuating physiological symptoms and perceptual sensations, especially when combined with menthol at lower temperatures (Riera *et al.*, 2014; Tran Trong *et al.*, 2015). If athletes cool the oral cavity during exercise, using cool liquid, ice, or even menthol, as in the works of Riera and Tran Trong (Riera *et al.*, 2014; Tran Trong *et al.*, 2015), cold receptors are stimulated in the oral cavity, conferring a hedonic effect and possibly satiating thirst (Eccles, 2000; Eccles *et al.*, 2013). Satiating thirst may also reduce the likelihood of gastrointestinal distress associated with ingesting large volumes of liquid, particularly when running (Lambert *et al.*, 2008). The role of menthol in facilitating ingested cooling methodologies also warrants further investigation (Stevens and Best, 2017).

Topical percooling lowers skin temperature, inducing cutaneous vasoconstriction and increasing the temperature gradient between the skin and the external environment in hot conditions (Cheuvront and Haymes, 2001). This mechanism permits convective and radiative heat exchange up to temperatures of 36 °C (Cheuvront and Haymes, 2001), beyond which evaporative cooling becomes the main method of body temperature regulation. Dry, windy conditions that promote convection and evaporation (Morris and Jay, 2016) are required for topical cooling to be most effective. The included topical percooling studies (Muñoz *et al.*, 2012; Schulze *et al.*, 2015) present practical ways of cooling athletes that are less cumbersome than typical precooling strategies, namely pouring cold water over the body and the application of cold towels. Both methods could

be easily transported in a cool box and kept roadside or trackside. The pouring of cold water is especially valid and practical, with many athletes already doing so in competition (Morris and Jay, 2016; Filingeri, 2016).

Skin wetness may also be important in cooling and is influenced by factors pertinent to athlete comfort during endurance exercise in the heat, such as humidity and airflow over the skin (Filingeri, 2016). In the absence of airflow over the skin, topical and combined methodologies applied within lab conditions improve thermal comfort and sensation by providing targeted stimuli that aggressively reduce local skin temperatures (Bongers *et al.*, 2014). Some topical methods may promote skin wetness (cold water and/ or towels) and therefore facilitate evaporative cooling, whereas others (ice vests) stimulate large, cold-sensitive areas such as the chest and back (Wendt, van Loon and Lichtenbelt, 2007; Bogerd *et al.*, 2010; Eijsvogels *et al.*, 2014; Filingeri, 2016), and reduce skin temperature very quickly, all important factors in improving thermal perceptions (Wendt, van Loon and Lichtenbelt, 2007).

Although no positive effects on time trial performance or power output were noted following topical or combined strategies, performance did not worsen either ((Stanley, Leveritt and Peake, 2010; Ross *et al.*, 2012; Schulze *et al.*, 2015); Table 3.2). There may be occasions where an attenuation of an athlete's perception of thermal state is beneficial, provided performance does not deteriorate (e.g., a domestique in the Tour de France, who must maintain a consistent level of performance over 21 days of riding, in rapidly changing thermal circumstances, with his performance tasks altering depending on the needs and strategies of his team day by day).

We found combining topical and ingested cooling methods to only have a trivial effect upon time trial performance with a broad confidence interval (-0.07 ; -0.44 to 0.29), supported by an expectedly trivial change in power output (0.02 ; -0.39 to 0.44). Combined cooling methods do, however, markedly lower rectal temperature whilst also improving thermal comfort and sensation, although they may inhibit physiological processes facilitative to endurance performance in the heat, such as increased vasodilation, muscular or skin blood flow, and sweating (Ouzzahra, Havenith and Redortier, 2012). The moderate reduction in rectal temperature seen when combining methodologies likely results in an insufficient temperature gradient between the core and skin, dampening the performance enhancing effects either treatment would promote in isolation. The breadth of the confidence intervals around the trivial performance effects of combined cooling methodologies may be explained in part by the individual, and regional variation in these

physiological responses, as well as the heterogeneity of study designs (Hopkins and Hewson, 2001; Hopkins, 2005; Stevens and Best, 2017).

The range of observed responses, as evidenced through broad confidence intervals, suggest that the timing and methodology employed can affect athletes' performances differently, and, more importantly, that differing strategies may target different mechanisms (i.e., a reduction in either perceived (Mündel and Jones, 2009; Stevens *et al.*, 2016; 2017; Stevens and Best, 2017) or physiological thermal load (Stanley, Leveritt and Peake, 2010; Ross *et al.*, 2012; Stevens *et al.*, 2013; Gonzales *et al.*, 2014; Stevens *et al.*, 2016; 2017), or both (Riera *et al.*, 2014; Tran Trong *et al.*, 2015)). Each targeted mechanism(s) likely possesses differing levels of intra- and inter-individual variability, and this may further vary between investigations, as per Figure 3.2 and Table 3.2. Quantifying the coefficient of variation in athletes' performances and associated measures (e.g., thermal comfort or sensation) is an important step in assessing the efficacy of an intervention. If an intervention produces a change that is greater than the coefficient of variation observed in an individual or group, it can be deemed to have had an effect. Several papers provide a good starting point for this analysis in cycling (Zavorsky *et al.*, 2007), running (Hopkins and Hewson, 2001; Hopkins, 2005; Hurst and Board, 2016), and triathlon (Paton and Hopkins, 2005), and Atkinson and Nevill (2001) provide a working example for the practitioner.

Finally, although beneficial in acute settings, little is known about the long-term application of cooling interventions in the absence of heat acclimation. Repeated exposure to extremes of temperature may be detrimental to long-term health (Cheung, Lee and Oksa, 2016), and if cooling strategies are employed to repeatedly facilitate such exposure over the course of a season or training cycle then athlete health should be monitored accordingly.

3.4.1 Conclusion

We found that ingested cooling methodologies show ecologically important small improvements in time trial performance when applied before and during endurance exercise bouts (Figure 3.2; Table 3.2). Improvements in time trial performance and power output may be attributable to differing mechanisms (perceptual or physiological cooling) depending upon the cooling strategy being administered (Wegmann *et al.*, 2012); further elucidation of these mechanisms and their effects upon performance and long-term health is still required (Flouris and Schlader, 2015; Roelands, De Pauw and Meeusen, 2015). Carbohydrate provision may be a confounding but contributory factor with respect to the investigation of cooling strategies as a means of performance enhancement.

When choosing a cooling strategy, we urge practitioners to consider the strategy's effects holistically, assessing athletes' perceptual and physiological responses to cooling in training prior to competition. Optimal frequency and timing of cooling strategies is likely a convergence of athletes' responses to cooling interventions and sport-specific statutory limitations (e.g., number of feed stations). Simply providing athletes with cool or cold water before and during events allows for athletes to ingest, swill, or pour the liquid over themselves, and therefore is a useful first step for providing cooling interventions. If practitioners can provide athletes with ice slurries for ingestion, this would likely further improve performance by ameliorating thermal comfort and sensation, and an attenuation of core temperature—the addition of menthol may support these effects.

Chapter 4 : MENTHOL: A FRESH ERGOGENIC AID FOR ATHLETIC PERFORMANCE²

The application of menthol has recently been researched as a performance enhancing aid for various aspects of athletic performance including endurance, speed, strength and joint range of motion. A range of application methods has been used including a mouth rinse, ingestion of a beverage containing menthol or external application to the skin or clothing via a gel or spray. The majority of research has focused on the use of menthol to impart a cooling sensation on athletes performing endurance exercise in the heat. In this situation, menthol appears to have the greatest beneficial effect on performance when applied internally. In contrast, the majority of investigations into the external application of menthol demonstrated no performance benefit. While studies are limited in number, menthol has not yet proven to be beneficial for speed or strength, and only effective at increasing joint range of motion following exercise that induced delayed onset muscle soreness. Internal application of menthol may provoke such performance enhancing effects via mechanisms related to its thermal, ventilatory, analgesic and arousing properties. Future research should focus on well-trained subjects and investigate the addition of menthol to nutritional sports products.

4.1 Introduction

The role of the brain in the regulation of exercise performance has received increasing attention across the last decade (Noakes, 2011). Opinion remains divided as to whether regulation occurs exclusively at the neurological level (Gibson and Noakes, 2004) or if interactions between various physiological and psychological feed-forward and feedback mechanisms to generate an athlete's feelings of self (Craig, 2003) and as such, fatigue whilst exercising (Marino, Gard and Drinkwater, 2009). What has been repeatedly demonstrated, however, is that physical performance can be modified through interventions acting exclusively on the central nervous system, for example, music (Karageorghis and Priest, 2012) experimenter sex (Lamarche, Gammage and Gabriel, 2011) and time or performance deception (H. S. Jones *et al.*, 2013). Various mouth rinsing techniques may also be performance enhancing, which involve briefly exposing the oral

² The work presented in this chapter has been accepted for publication in Sports Medicine doi: 10.1007/s40279-016-0652-4.

cavity to a stimulus (e.g. carbohydrate, caffeine, menthol) with the intention to induce afferent feedback to the brainstem that may ameliorate fatigue (Burke and Maughan, 2014).

Carbohydrate mouth rinsing has been the main strategy studied to date, with it being postulated that the brief exposure of carbohydrate to the oral cavity elicits neurological responses associated with imminent nutrient availability (Simon *et al.*, 2006), reward (Chambers, Bridge and D. A. Jones, 2009) and motor output (Chambers, Bridge and D. A. Jones, 2009). These findings led to the emergence of other mouth rinsing strategies (Burke and Maughan, 2014) including menthol (Mündel and D. A. Jones, 2009). A menthol mouth rinse is used to impart sensations of coolness, freshness and nasal patency through stimulation of the trigeminal nerve (Naito *et al.*, 1997; Eccles, 2000) and as an agonist to the TRPM8 channel which serves as a cold temperature sensor (Patel, Ishiuchi and Yosipovitch, 2007). These mechanisms and resultant sensations explain menthol's prolific use as a flavouring and fragrance agent in confectionary and medications (Eccles, 1994).

Considering hotter perceptions of thermal sensation and discomfort negatively affect endurance exercise performance (Schlader *et al.*, 2011) and menthol has a perceptual cooling effect (Eccles, 2000), it may be useful as an ergogenic aid for athletic performance, especially in hot environmental conditions (Stevens, Taylor and Dascombe, 2016). Additionally, menthol has been proposed as a cooling and analgesic compound useful for application on injured and/or sore muscles, to promote recovery and enhance subsequent contraction force (Johar *et al.*, 2012). With a vast range of application methods, dosages, exercise protocols and performance outcomes however, the beneficial effect of menthol on athletic performance seems equivocal. Hence, the current review aims to provide recommendations for athletes using menthol to enhance athletic performance. The psychophysiological mechanisms of action will also be explored and directions will be provided for future research.

4.2 Literature Search Methods

Searching was carried out within the databases *PubMed* and *Scopus* up to October, 2016. Search terms included menthol, L-menthol, mint, peppermint, counterirritant, cooling, exercise, performance and thermal sensation. Inclusion criteria stipulated that investigations must be written in English and have implemented a menthol-based intervention on a measured aspect of athletic performance. Subjects of all abilities were

included and while the majority of studies were performed in a hot environment ($>30^{\circ}\text{C}$), investigations performed in neutral-warm environments ($20\text{-}30^{\circ}\text{C}$) were also included.

4.3 Menthol and Athletic Performance

To date, the use of menthol as an ergogenic aid for athletic performance has taken the form of a mouth rinse (Stevens, Thoseby, *et al.*, 2016), an additive to other beverages (Riera *et al.*, 2014; Tran Trong *et al.*, 2015) or as a gel or spray applied externally to the skin or clothing (Kounalakis *et al.*, 2010; Barwood *et al.*, 2015). Hence, it is either applied internally or externally. Importantly, the degree of the cooling sensation from menthol to a body area correlates inversely with the thickness of the stratum corneum, where a thicker stratum corneum is a more difficult barrier to penetrate (Watson *et al.*, 1978). The density of cold-sensitive afferents on a particular body segment will also influence the degree of the cooling sensation from menthol application. Hence, for the same menthol dose, the tongue and oral cavity are more sensitive to menthol in comparison to the torso (Watson *et al.*, 1978) and as such, the effects of menthol application on the oral cavity (internal) will be discussed separately to application on the skin (external).

4.3.1 Internal Application of Menthol and Athletic Performance

A summary of research determining the effect of internal menthol application on physical capacity and performance appears in Table 4.1. A novel strategy is to simply rinse (or swill) the mouth with a liquid menthol solution prior to spitting out the solution. In the first study of its kind, a menthol mouth rinse (25 mL at a concentration of 0.01% performed every 10 min) significantly improved cycling time to exhaustion by 9% (Mündel and D. A. Jones, 2009). The researchers also observed significantly increased expired air volume, highlighting a greater drive to breath and/or lowered airway resistance, as well as a lower rating of perceived exertion. Similar findings have also been observed within running time trials in the heat, where menthol mouth rinse (25 mL at a concentration of 0.01% performed every 1 km) significantly improved 5 km performance time by 3% (Stevens, Thoseby, *et al.*, 2016) and 3 km performance time by 3.5% when combined with a facial water spray (Stevens, Bennett, *et al.*, 2016). Across these studies, significantly increased expired air volume was also observed alongside significantly cooler thermal sensation (Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016). Notably, the use of a menthol mouth rinse performed during exercise, whether combined with facial water spray or not, was significantly more beneficial for running time trial performance in the heat compared to the use of well established pre-cooling strategies (Stevens, Bennett, *et al.*,

2016; Stevens, Thoseby, *et al.*, 2016). As such, a menthol mouth rinse performed intermittently during exercise appears to be an effective intervention to improve endurance exercise performance in the heat.

Two promising investigations on internal menthol application and endurance performance have involved ingesting a menthol-aromatized beverage (Riera *et al.*, 2014; Tran Trong *et al.*, 2015). Riera *et al.*, (2014) performed several comparisons of different menthol-aromatized beverages that were ingested prior to and every 5 km during a 20 km cycling time trial in the heat. Menthol-aromatized beverages at 23°C, 3°C and ice slurry at -1°C were compared to a beverage of the same volume and temperature without menthol (Riera *et al.*, 2014). The addition of menthol to the 3°C beverage significantly improved performance time by 9%, while no significant differences were observed in the other conditions. Importantly, however, menthol-aromatized ice slurry was the most beneficial intervention compared to a 23°C control beverage without menthol. Similar studies out of the same laboratory have also demonstrated that the combination of menthol and ice slurry significantly improved performance in a simulated duathlon in hot conditions compared to other beverages also containing menthol at 28°C and 3°C, by 6% and 3%, respectively (Tran Trong *et al.*, 2015). Hence, the addition of menthol to a beverage ingested immediately prior to and during endurance exercise has a performance enhancing effect, and like the menthol mouth rinse, this strategy is not further enhanced by pre-cooling (Riera *et al.*, 2016). For the best outcome, menthol should be added to an ice slurry mixture to maximize cooling. Practically, however, recent research has demonstrated that when given the choice, athletes drink less ice slurry than cold fluid during a cycling time trial, which may contribute to deteriorated performance and feeling state (Maunder, Laursen and Kilding, 2016).

Other investigations into menthol ingestion and sports performance have taken the form of peppermint ingestion, which typically contains a high concentration of menthol (Sönmez *et al.*, 2010; Meamarbashi and Rajabi, 2013; Meamarbashi, 2014). No performance improvements were gained in an outdoor 400 m running time trial following the ingestion of 5 mL·kg⁻¹ of peppermint extract (50 g of dried mint infused into 1 L of water for 15 min) (Sönmez *et al.*, 2010). Hence, this initial study suggests menthol may not be an effective aid for such short duration activity, but more research is needed to confirm this notion. Other studies to investigate the use of peppermint ingestion as a pre-exercise ergogenic aid (Meamarbashi, 2014) or an oral supplement consumed every day for 10 days (Meamarbashi and Rajabi, 2013) were tarnished by failing to implement a cross-over design or failing to include a control trial, respectively.

Table 4-1 Summary of research determining the effect of internal menthol application on physical capacity and performance.

Investigation	Ambient Conditions	Subjects	Menthol Application Method	Protocol	Outcome
Mundel and Jones (2009)	34°C, 27% RH	9 males, $VO_{2max} = 54 \pm 5 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	Menthol mouth rinse (25 mL at 0.01% every 10 min)	Cycling TTE at 65% VO_{2max}	↑ TTE by 5 min (9%) ↑ VE, ↓ RPE
Sönmez et al. (2010)	NR	16 (sex NR), untrained	Oral mint extract (5 mL·kg) ingested prior to performance test	Running TT of 400 m	↔ Perf time ↓ BLA, ↔ muscle pain
Riera et al. (2014)	31°C, 78% RH	12 males, $VO_{2max} = 60 \pm 10 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	Ingestion of beverage with/without menthol (190 mL at 0.05% 3 x prior and every 5 km during exercise) at a) 23°C; b) 3°C; or c) -1°C ice slurry	15 min cycle at ventilatory threshold one then 20 km TT	a) ↔ Perf time b) ↑ Perf time by 3 min (9%) c) ↔ Perf time ↔ HR, RPE, TC or TS
Tran Trong et al. (2015)	28°C, 57% RH	10 males, $VO_{2max} = 59 \pm 11 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	Ingestion of a menthol aromatized beverage (190 mL at 0.05% during WU, every interval and recovery) at a) 3°C; or b) 0.2°C ice slurry, compared to 28°C fluid	15 min cycle WU then 5 x intervals of (4 km cycle and 1 km running TT)	a) ↔ Perf time b) ↓ Perf time by 5 min (6%) and ↓ perf time by 2 min (3%) compared to 'a' ↔ HR, RPE, TC or TS
Stevens et al. (2016)	33°C, 46% RH	11 males, 5 km run time of 18-22 min	Menthol mouth rinse (25 mL at 0.01% every 1 km)	10 min walk/run on NMT then running TT of 5 km on NMT	↓ Perf time by 0.7 min (3%) ↓ TS, ↑ VE, ↑ PRL, ↔ SR
Stevens et al. (2016)	33°C, 47% RH	11 males, $VO_{2max} = 61 \pm 6 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	Menthol mouth rinse (25 mL at 0.01% every 4 min/1 km) and facial water spray (every 4 min/1 km)	20 min run at 70% VO_{2max} on NMT then running TT of 3 km on NMT	↓ Perf time by 0.5 min (3.5%) ↓ TS, ↓ T_F , ↓ PRL, ↑ VE, ↔ SR

Riera et al. (2016)	WBGT: 29°C, 80% RH	9 males, $\text{VO}_{2\text{max}} = 59 \pm 11 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	Ingestion of menthol aromatized ice slurry during exercise (7 mL·kg at 0.03%) with vs. without pre-cooling with cold water (7 mL·kg at 3°C)	10 min cycle at ventilatory threshold one then 30 km time trial	↔ Perf time ↔ TS, TC, HR, RPE, T_{CORE}
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↔ = no change, BLa = blood lactate concentration, HR = heart rate, NMT = non-motorized treadmill, NR = not reported, perf = performance, PRL = blood prolactin concentration, RH = relative humidity, RPE = rating of perceived exertion, SR = sweat rate, TC = thermal comfort, T_{CORE} = core temperature, T_{F} = forehead temperature, TS = thermal sensation, TT = time-trial, TTE = time to exhaustion, VE = volume of expired air, $\text{VO}_{2\text{max}}$ = maximal oxygen uptake, WBGT = wet blub globe temperature, WU = warm-up.

Table 4-2 Summary of research determining the effect of external menthol application on physical capacity and performance.

Investigation	Ambient Conditions	Subjects	Menthol Application Method	Protocol	Outcome
Schlader et al. (2011)	20°C, 48% RH	12 males, untrained	Topical application of menthol gel on the face (0.5 g•100 cm ² at 8% prior to protocol)	Cycling TTE RPE clamp protocol at 16 'hard-very hard'	↑ Total work by 39 kJ (21%) ↓ TS, ↑ TC
Topp et al. (2011)	NR	9 males, 8 females, untrained	Topical application of menthol gel on the right forearm (3.5 g total: 0.5 g•100 cm ² at 3.5% 20 min prior to protocol)	30 repeated maximal flexions and extensions of the wrists at 30°•s	↔ Muscle strength ↓ Blood flow in radial artery
Johar et al. (2012)	NR	12 males, 4 females, untrained	Topical application of menthol gel on the <i>Biceps Brachii</i> (2 g total: 0.5 g•100 cm ² at 3.5% 20 min prior to protocol)	MVC and EF of the elbow flexors 48 h post DOMS inducing exercise	↔ MVC or EF ↓ Perception of DOMS
Barwood et al. (2012)	32°C, 50% RH	11 males, 40 km cycle time < 70 min	Menthol sprayed on the cycling jersey (106 mL at 0.05% between WU and TT)	Cycling TT of 40 km	↔ Perf time ↓ TS, ↑ TC
Barwood et al. (2014)	34°C, 50% RH	6 males, untrained	Menthol sprayed on the running top (100 mL at 0.05% between pre-load and TT)	15 min fixed intensity pre-load run then 5 km TT	↔ Perf time ↓ TS, ↑ TC
Barwood et al. (2015)	34°C, 33% RH	8 males, untrained	Menthol sprayed on the cycling jersey (100 mL at 0.2% after 10 km of TT)	Cycling TT of 16.1 km	↔ Perf time ↓ RPE, ↓ TS, ↑ TC

↔ = no change, DOMS = delayed onset muscle soreness, EF = evoked force, NR = not reported, MVC = maximal voluntary contraction, perf = performance, RH = relative humidity, RPE = rating of perceived exertion, TC = thermal comfort, TS = thermal sensation, TT = time-trial, TTE = time to exhaustion, WU = warm-up.

4.3.2 External Application of Menthol and Athletic Performance

A summary of research determining the effect of external menthol application on physical capacity and performance appears in Table 4.2. Half of these investigations have involved the spraying of a menthol solution onto the exercise clothing either prior to (Barwood *et al.*, 2012; Barwood, Corbett and White, 2014) or during an endurance exercise time trial (Barwood *et al.*, 2015). Spraying a menthol solution on the exercise clothing at a concentration of 0.05% resulted in no improvements in 40 km cycling time trial performance (Barwood *et al.*, 2012) or 5 km running time trial performance (Barwood, Corbett and White, 2014) despite significantly cooler thermal sensation and improved thermal comfort in both instances. The spray was also ineffective when the menthol solution was more concentrated (0.2%) and implemented at the 10 km mark of a 16.1 km cycling time trial, despite lower ratings of perceived exertion, cooler thermal sensation and improved thermal comfort (Barwood *et al.*, 2015). Only one study has demonstrated a beneficial performance effect of an external menthol application when a menthol gel at 8% concentration was applied to the face in a volume of 0.5 g·100 cm² (Schlader *et al.*, 2011). This intervention increased total work completed by 21% in a cycling time to exhaustion protocol at a fixed rating of perceived exertion and was also accompanied by significantly cooler thermal sensation and improved comfort. As such, the external application of menthol may need to be applied directly to the face, or at least directly to the skin at a high concentration in order to have an ergogenic effect. It should be noted, however, that the perceptually driven protocol may be more likely to be affected by an intervention designed to influence perception and hence, further investigation into the application of menthol on the face is needed.

Other investigations that have applied a menthol gel directly to the skin have assessed the effects on muscle strength (Johar *et al.*, 2012; Topp *et al.*, 2011) and joint range of motion (Akehi and Long, 2013; Haynes and Perrin, 1992). A menthol gel applied to the forearm at a concentration of 3.5% and a volume of 0.5 g·100 cm² did not improve isokinetic muscle strength 20 minutes after application (Topp *et al.*, 2011). Similarly, a menthol gel with the same concentration and volume applied to the *biceps brachii* did not improve maximal voluntary contraction or evoked force of the elbow flexors 20 minutes after application and 48 hours after exercise that induced delayed onset muscle soreness (Johar *et al.*, 2012). In regards to joint range of motion, one investigation demonstrated that application of a 2% menthol gel increased range of motion of the elbow joint following an eccentric exercise protocol to induce delayed onset muscle soreness (Haynes and Perrin, 1992), however, application of a 16% menthol gel did not affect hamstring range of motion

in absence of preceding eccentric exercise (Akehi and Long, 2013). Therefore, the use of a topical menthol gel appears to have little influence on muscle strength and joint range of motion in the recovered state.

4.4 Mechanisms of Action

The application of menthol for the improvement of endurance performance in the heat has been proposed to induce several psychophysiological adjustments including thermal (Gillis *et al.*, 2016), ventilatory (Stevens, Thoseby, *et al.*, 2016), analgesic (Johar *et al.*, 2012) and arousal effects (Smith and Boden, 2013).

4.4.1. Thermal Effect

Improved feelings of thermal comfort and sensation are observed when menthol is applied topically (Schlader *et al.*, 2011; Barwood *et al.*, 2012; Barwood, Corbett and White, 2014; Barwood *et al.*, 2015) and when administered orally (Stevens, Thoseby, *et al.*, 2016; Stevens, Bennett, *et al.*, 2016). Researchers investigating topical application of menthol often apply garments that have been treated with low concentration menthol solutions. This facilitates evaporative cooling and stimulation of cold receptors by placing the garment and menthol in contact with large, cold sensitive areas such as the chest and back (Filingeri, 2016). Specifically, the solvent (typically water and alcohol) evaporates as a result of an increased rate of heat production and skin temperature during exercise, whilst menthol stimulates cold sensitive TRPM8 receptors, creating a subjective feeling of coolness (Eccles, 2000a). Menthol has, however, also been shown to promote a heat storage response during exercise (Gillis, House and Tipton, 2010; Gillis *et al.*, 2016) and at rest (Valente *et al.*, 2015) due to perturbed sweat rate (Kounalakis *et al.*, 2010) and vasoconstriction of blood vessels (Valente *et al.*, 2015; Gillis *et al.*, 2015). These thermoregulatory responses may explain why topical application of menthol is not beneficial for endurance performance in the heat when applied to large areas, prior to or during an intense and prolonged bout of exercise (Valente *et al.*, 2015). When menthol is applied to smaller areas, such as the face, these physiological responses are not observed, yet cooler thermal sensation and improved thermal comfort still occur (Schlader *et al.*, 2011). However, the disassociation between the physiological and perceptual responses to body heat from topical menthol application presents an ethical consideration for researchers, as it may permit exercise beyond normal thermal limits and an increase in the stress hormone prolactin (Stevens, Thoseby, *et al.*, 2016). Application of menthol close to the onset of hyperthermia should be avoided to allow perception of symptoms associated

with high levels of heat stress, adjustment to self-selected exercise intensity and the prevention of heat injury.

When administered orally, menthol evokes pleasant and refreshing sensations of airflow and nasal patency, improving thermal comfort and sensation by acting as an afferent to the palatine and trigeminal nerves (Eccles, 1994; Valente *et al.*, 2015). Despite performance improvements with oral menthol supplementation when used in conjunction with other cooling methods, thermal perception was not cooler in protocols performed outside of the laboratory (Riera *et al.*, 2014; Tran Trong *et al.*, 2015). Such a finding suggests that in the presence of airflow, oral application of menthol improves performance by mechanisms beyond improvements in thermal perception.

4.4.2. Ventilatory Effect

Menthol consistently increases ventilation in the form of expired air volume (Mündel and D.A. Jones, 2009; Stevens, Bennett *et al.*, 2016; Stevens, Thoseby *et al.*, 2016) when administered as a liquid mouth rinse (0.01%) with concomitant improvements in running performance (Stevens, Bennett *et al.*, 2016; Stevens, Thoseby *et al.*, 2016) and cycling time to exhaustion (Mündel and D.A. Jones, 2009). While at rest, oral application of menthol inhibits the drive to breathe (Eccles, 2000) and decreases the discomfort experienced during breathing with a restrictive load (Nishino, Tagaito and Sakurai, 1997), serving to reduce ventilation (Fisher, 2011). Therefore, since exercise increases the ventilatory requirements of the body, at times to a near maximal level (Blackie *et al.*, 1991), oral administration of menthol during exercise can lower perceived cardiopulmonary exertion (Mündel and D.A. Jones, 2009) which may allow an overall greater depth and/or rate of breathing. However, there is no evidence that menthol has the capacity to decrease physical airway resistance (Naito *et al.*, 1997; Kenia, Houghton and Beardsmore, 2008), suggesting the effect is perceptual only (Nishino *et al.*, 1997; Pereira, Sim and Driver, 2013).

4.4.3. Analgesic Effect

Menthol has been used for medicinal purposes since ancient times (Patel *et al.*, 2007) and more recently, it has been suggested to have an analgesic effect for sports injuries, delayed onset muscle soreness and arthritis (Eccles, 1994; Johar *et al.*, 2012) and hence its inclusion in many topical creams to reduce musculoskeletal pain. Aside from its cooling

effect through the TRPM8 channel, menthol has been demonstrated to inhibit the TRPA1 channel, a mediator of inflammatory pain (Macpherson *et al.*, 2006). While topical application of menthol (3.5%) decreased perceived pain and improved physical function in patients with knee osteoarthritis (Topp, Brosky and Pieschel, 2013), research to date has not investigated the analgesic effects of menthol during exercise in athletes.

4.4.4. Arousal Effect

Menthol has also been suggested to have arousing properties similar to the feeling of cold air on the face when drowsy (Eccles, 2000). Chewing menthol gum has been associated with improved mental alertness (Smith and Boden, 2013) and breathing a menthol fragrance through a mask increased vigilance in a sustained visual attention task (Warm, Dember and Parasuraman, 1991). In contrast however, chewing on a menthol lozenge failed to enhance mood ratings of alertness, hedonic tone and tension during simulated firefighting in the heat (Zhang *et al.*, 2014). As such, further research is needed to determine if arousal plays a role in the improvement of endurance exercise performance in the heat from internal menthol application.

4.5. Practical Recommendations

Endurance athletes competing in the heat are recommended to experiment with internal menthol application methods both pre-and mid-exercise. This may take the form of a mouth rinse or a beverage containing menthol by adding 0.1-0.5 g of crushed menthol crystals, dissolved in alcohol, to 1 L of water. Alternatively, a pre-mixed L-menthol/alcohol solution that is available commercially as a food additive can be used in the same quantity. Athletes should experiment with different concentrations of menthol in their beverages to find individual limits that are both tolerable and beneficial to performance. Indeed, all attempts at internal menthol application should be trialled thoroughly within mock competition scenarios at race intensities to ensure no adverse consequences are to occur in a race situation.

4.6. Directions for Future Research

To improve translation for athletes, future research into menthol and sports performance should recruit well-trained subjects. Only half of the investigations presented in Tables 1-2 used trained or well-trained subjects, which is known to improve test reliability (Stevens and Dascombe, 2015) and is also important to understand the specific responses within this population. It should be noted that for the studies concerning the internal application

of menthol and endurance performance, the researchers formulated their own liquid menthol solution for mouth rinsing or ingestion. Hence, development of an optimal solution for these purposes is needed, and further, experimentation with combinations of menthol, carbohydrate, electrolyte and caffeine would increase practicality for athletes. Synthetic compounds with similar cooling effects should also be considered as they may have improved palatability and may be easier to formulate (Watson *et al.*, 1978) Future researchers should ensure that the dose of any external solution is specified (in g·cm²) to simplify comparisons between studies and further, assessment of the dose-response relationship is also needed for the various menthol application methods. Finally, current research has focussed on the thermal and ventilatory mechanisms of internal menthol application, while the analgesic and arousing properties of menthol may also contribute to improved endurance exercise performance in the heat. Hence, these measures should be incorporated into future research.

4.7. Conclusion

The majority of research has focused on the use of menthol to impart a cooling sensation on athletes performing endurance exercise in the heat. In this situation, menthol appears to have the greatest beneficial effect on performance when applied internally. Conversely, only one study observed an improvement in endurance exercise capacity following external application of menthol. While studies are limited in number, menthol has not yet proven to be beneficial for speed or strength and only effective at increasing joint range of motion following exercise that induced delayed onset muscle soreness. Internal application of menthol likely stimulates improvements in endurance performance in the heat through thermal and ventilatory mechanisms, however the analgesic and arousing properties of menthol may also play a role.

CHAPTER 5 : THE DEVELOPMENT OF A MENTHOL SOLUTION FOR USE DURING SPORT AND EXERCISE³

Menthol mouth-swilling has been shown to improve performance across differing exercise modalities, yet no work has been conducted to ascertain the preferred concentration of menthol within a swill. Colour has also been shown to influence psychophysiological outcomes, and may influence the efficacy of ergogenic aids. We conducted two experiments: one to ascertain preferred menthol concentration (0.005-0.105% menthol), the second to assess colour preference (Light Blue, Dark Blue, Light Green, Dark Green, Red). Participants rated swills for Smell, Taste, Freshness, Mouth Feel and Irritation (plus Appearance in the second trial) via 15cm Visual Analogue Scales (VAS), having swilled and expectorated 25ml of fluid. Both trials employed a crossover design, with tasting order assigned by Latin squares. Differences were assessed for statistical significance ($p < 0.05$) using one way repeated measures ANOVAs. Standardised mean differences \pm 90% confidence intervals were calculated to assess the magnitude of any observed differences. No significant differences were found between concentrations for total VAS score, but higher concentrations demonstrated a greater number of small effects. Similarly, no significant differences between colours were found. Small effects were found when Light Green was compared to Dark Green and Red. Effects were trivial when Light Green was compared to Light Blue (0.05 ± 0.20) and Dark Blue (0.19 ± 0.32). We recommend athletes employ a Light Green or Light Blue 0.1% menthol mouth-swill.

5.1 Introduction

Mouth-swilling strategies may be useful during exercise to alleviate 'dry mouth' brought about by a reduction in salivary flow rate (Dawes, 1987). Other ergogenic effects are likely dependent upon the exercise mode undertaken (Beaven *et al.*, 2013; Clarke, Kornilios and Richardson, 2015; Stevens and Best, 2017; Peart, 2017) and active ingredients within the swill, e.g., Caffeine (Beaven *et al.*, 2013; Doering *et al.*, 2014), Carbohydrate (Burke and Maughan, 2014; Stellingwerff and Cox, 2014) or Menthol (Stevens and Best, 2017). These ingredients may also be combined with other ergogenic strategies to maximise the

³ The work presented in this chapter has been accepted for publication in the journal *Beverages* doi: <https://doi.org/10.3390/beverages4020044>

influence upon physiological and psychological determinants of fatigue (Riera *et al.*, 2014; Tran Trong *et al.*, 2015; Best *et al.*, 2018).

Menthol presents in nature as both a fragrance and flavour molecule, targeting the olfactory and gustatory systems (Eccles, 1994; 2000), typically imparting feelings of coolness and freshness (Eccles, 1994; 2000; Eccles *et al.*, 2013), hence its seemingly ubiquitous use in consumable products such as confectionary, cosmetics and pharmaceutical applications. A more contemporary application of menthol has been that of an ergogenic aid which can be applied topically (Gillis *et al.*, 2016), used as a mouth swill (Mündel and Jones, 2009; Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016) or ingested alongside ice slurry (Riera *et al.*, 2014; Tran Trong *et al.*, 2015; Riera *et al.*, 2016). This use is fitting, with menthol shown to increase the drive to breathe (Eccles, 2003), elevate ventilation (Meamarbashi and Rajabi, 2013) and attenuate thirst (Eccles, 2000), along with eliciting sensations of coolness and freshness that may alleviate thermal symptoms during exercise (Stevens and Best, 2017). However, the variability of concentration of menthol within mouth swills and other menthol containing strategies applied to the oral cavity is large. Given such variability, the potential for menthol concentration to affect the efficacy of a treatment, palatability of the menthol solution and any resultant physiological or subjective effects brought about by menthol use is viable. Therefore, an optimal or preferred concentration should be explored.

Similar to concentration, colour has been shown to influence the efficacy of a treatment. For example, studies assessing medical interventions (de Craen *et al.*, 1996), product design (Fenko, Schifferstein and Hekkert, 2010), solution odour (Michael and Rolhion, 2008) and fictitious sport supplements (Szabo *et al.*, 2013) have reported that the colour of the treatment can significantly influence psychophysiological outcomes. The colour green has been associated with coolness (Michael and Rolhion, 2008; Fenko, Schifferstein and Hekkert, 2010), tranquilising effects (de Craen *et al.*, 1996) and enhanced endurance performance (Szabo *et al.*, 2013), with blue displaying similar qualities (de Craen *et al.*, 1996; Michael and Rolhion, 2008; Fenko, Schifferstein and Hekkert, 2010). Conversely, red and orange are renowned for stimulatory and warming effects (de Craen *et al.*, 1996; Fenko, Schifferstein and Hekkert, 2010) but have been shown to decrease motor performance (Briki *et al.*, 2015). Such responses are thought to be conditioned through previous experience of colour-associated treatments (de Craen *et al.*, 1996; Fenko, Schifferstein and Hekkert, 2010), suggesting that previous experience with a coloured product or intervention, may influence participants expectation about the efficacy of that treatment (de Craen *et al.*, 1996; Szabo *et al.*, 2013).

Menthol's novel properties, when coupled with the potential for colour to enhance perceptions of coolness and treatment efficacy, suggest that the development of a menthol solution for experimental application is a process that requires consideration, beyond that of palatability. Therefore, the aims of this study were twofold: (1) to ascertain the preferred concentration of a menthol solution, and (2) to identify preferred colour of a menthol solution. To achieve this, we conducted two separate experiments.

5.2 Material and methods

Two repeated measures, post-only crossover design studies were conducted. In study 1, twenty-one participants (15 male, 6 female, 26.9 ± 5.7 years) were recruited to understand the preferred concentration of menthol. In study 2, thirty-five participants (13 males, 22 females, 22.7 ± 5.7 years) were recruited to identify the preferred colour of a menthol solution. Both studies took place in laboratories at 22 ± 0.3 °C.

Participants in both experiments were excluded if they had any illness that affected their ability to taste or smell, they had anosmia (loss of smell), ageusia (loss of taste), or if they had recently suffered any stomach illnesses such as food poisoning or diarrhoea. Participants were also excluded if they were colour blind. Ethical approval was granted by the School of Social Sciences, Humanities and Law Ethics Committee at Teesside University.

In study 1, menthol crystals ((-)-menthol, Sigma Aldrich, Dorset, UK) were dissolved in ethanol to produce a 5% menthol solution (i.e., 50 g menthol per Litre of ethanol). Ethanol was used as a solvent to ensure thorough dilution of menthol throughout the solution, avoiding a film forming or any clumping of partially dissolved menthol crystals. The ethanol-menthol solution was then diluted to the experimental concentrations, using distilled water. Experimental concentrations ranged from 0.005 to 0.105%, in 0.01% increments. All solutions were colourless/transparent. Participants swilled 25 mL of menthol solution for 10 s (Mündel and Jones, 2009). They were then asked to rate the solution for *Smell, Taste, Mouth Feel, Freshness & Irritation*, using 15 cm Visual Analogue Scales (VAS). VAS were marked with polarised descriptors 'Unpleasant' and 'Pleasant' at the left and rightmost extremes of each scale, respectively. This process was repeated for each menthol concentration, with tasting order being assigned via an 11×11 Latin Square, through a custom-made spreadsheet. Water was available ad libitum between tastings. Coffee beans were made available to participants between trials. Inhaling the aroma from the beans provided a contrasting aromatic and olfactory stimulus, with a view to minimising cumulative sensory interference across menthol trials.

In study 2, coloured versions (light blue, dark blue, light green, dark green and red) of the preferred menthol solution identified in study 1 were tasted to assess the effect of colour on participants' perception of solution characteristics. Dark blue and green colours were achieved by adding 2 mL of food colouring (Queen Fine Foods Ltd., Alderley, Queensland, Australia) to solution, whereas light blue and green were produced by adding 0.5 mL of food colouring. The red solution contained 1 mL of food colouring to be independent of green and blue coloured solutions. Participants repeated the VAS as described in study 1, but in addition, were asked to rate the solutions' Appearance. Tasting order was assigned via a 5×5 Latin Square, through a custom-made spreadsheet.

Total VAS score (mean \pm standard deviation) per solution was calculated as the sum of the mean scores for each assessed variable, for each concentration and colour. One-way, repeated measures ANOVAs were used to assess the difference in total solution score, between solution concentrations and colour in study 1 and 2, respectively. Checks for normality and variance of the residuals were performed. All analyses were performed using SPSS (v23, IBM, New York, NY, USA). Effect sizes were calculated as standardised mean differences and 90% Confidence Intervals (C.I.) using a customised spreadsheet (Hopkins, 2006), with accompanying descriptors (Hopkins *et al.*, 2009). Effect Size thresholds are *Trivial* (>0.20) *Small* (0.2–0.6) *Medium* (0.6–1.2) *Large* (1.2–2.0) *Very Large* (>2.0) as per Hopkins and colleagues (Hopkins *et al.*, 2009). Ninety percent (90%) C.I. are used to differentiate between any observed significant results, and the likely range in which true differences may occur (Sterne and Smith, 2001; Hopkins *et al.*, 2009), rather than as another method of expressing a significant result.

5.3 Results

5.3.1 Solution concentration

Mauchly's test indicated that sphericity had been violated, $\chi^2(54) = 94.11$, $p = 0.001$; therefore, a Greenhouse-Geisser ($\epsilon = 0.470$) correction was applied. There were no significant main differences between menthol mouth swill concentrations, $F(4.695, 93.903) = 0.974$, $p = 0.435$. Standardised mean differences are presented in Table 1. Menthol concentrations of 0.095% and 0.105% demonstrated a greater number of Small effects than other concentrations; specifically, demonstrating Small effects with confidence intervals that did not overlap zero, and values for subjective overall perception of 389 ± 94.73 and 383.14 ± 107.22 , respectively (Figure 1; Panel A). Consequently, a 0.10% solution was used in the colour trial.

5.3.2 Solution colour

Mauchly's test indicated that sphericity had been violated, $\chi^2(9) = 24.08$, $p = 0.004$; therefore, a Greenhouse-Geisser ($\varepsilon = 0.755$) correction was applied. No significant differences were observed between mouth swill colours, $F_{(3.019, 11211.266)} = 0.835$, $p = 0.479$. Light Green was rated more highly than other solutions (Figure 2), and demonstrated Small differences against Dark Green ($0.28 \pm 90\% \text{ CI: } 0.33$) and Red (0.24 ± 0.31) but was only trivially different to Dark Blue (0.19 ± 0.32) and Light Blue (0.05 ± 0.20) solutions. Light Blue displayed a Small difference when compared to Dark Green (0.23 ± 0.38), with all other differences considered Trivial (Dark Blue: 0.14 ± 0.36 ; Red: 0.19 ± 0.32).

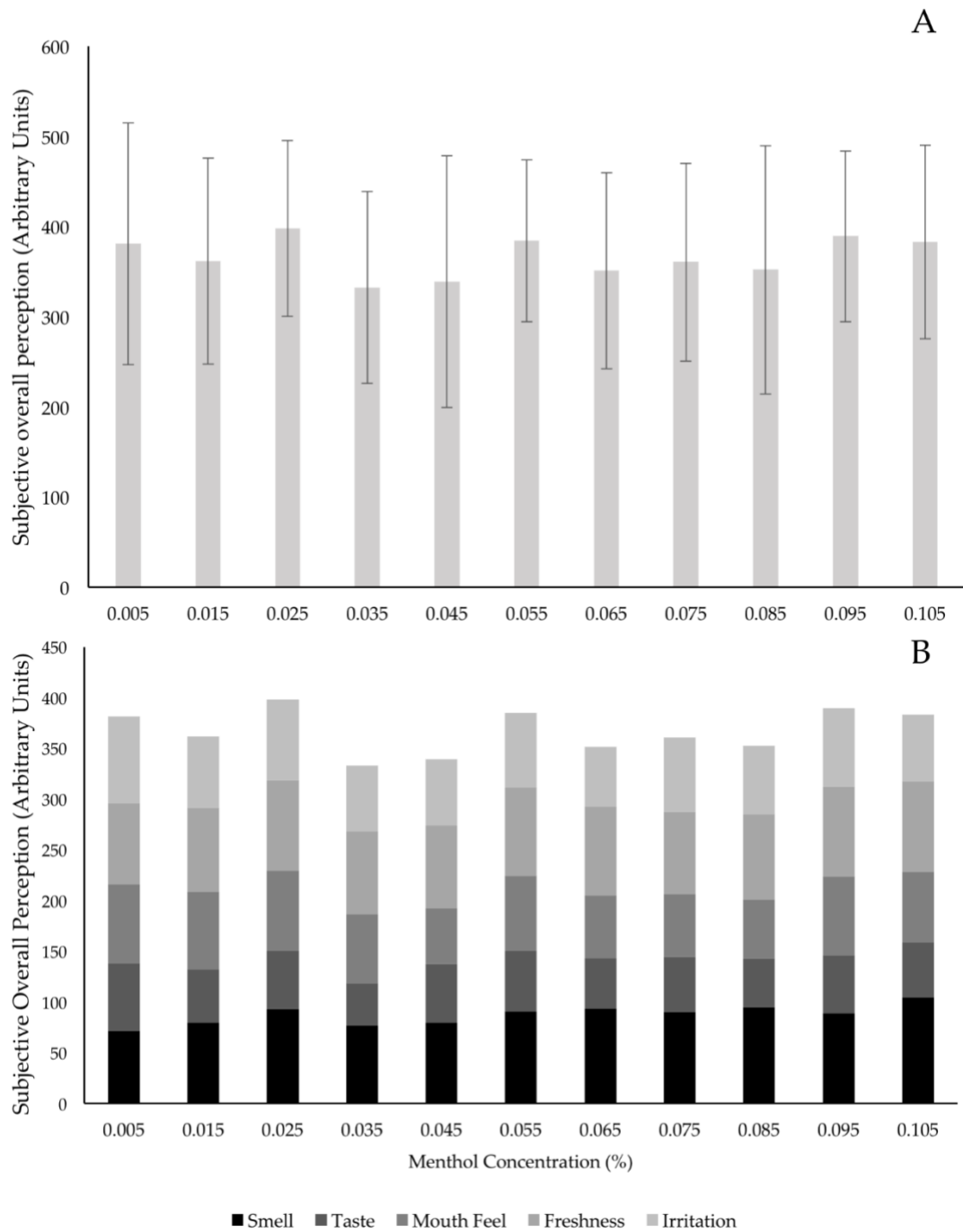


Figure 5-1 Subjective overall preference for each menthol concentration (%), expressed as Mean VAS rating per solution concentration \pm 1 S.D (Panel A) and as a sum of constituent mean VAS for each reported characteristic (Panel B).

Table 5-1 Effect Sizes and accompanying 90% Confidence Intervals for solution concentrations. Effect Size thresholds are Trivial (>0.20) Small (0.2 - 0.6) Medium (0.6 – 1.2) Large (1.2 – 2.0) Very Large (>2.0) as per Hopkins (2010). Small effects with confidence intervals not overlapping zero are marked with an asterisk (*).

	0.005	0.015	0.025	0.035	0.045	0.055	0.065	0.075	0.085	0.095	0.105
0.005	X	0.27 ± 0.56	0.03 ± 0.59	0.52 ± 0.59	0.49 ± 0.54	0.16 ± 0.48	0.44 ± 0.5	0.29 ± 0.58	0.41 ± 0.35*	0.09 ± 0.48	0.20 ± 0.55
0.015	-	x	0.29 ± 0.32	0.24 ± 0.24	0.19 ± 0.26	0.2 ± 0.39	0.09 ± 0.37	0.01 ± 0.39	0.08 ± 0.51	0.23 ± 0.48	0.17 ± 0.44
0.025	-	-	x	0.24 ± 0.25	0.19 ± 0.27	0.19 ± 0.36	0.08 ± 0.31	0.01 ± 0.35	0.08 ± 0.49	0.24 ± 0.52	0.19 ± 0.47
0.035	-	-	-	x	0.05 ± 0.37	0.44 ± 0.36*	0.16 ± 0.35	0.25 ± 0.32	0.41 ± 0.39*	0.50 ± 0.48*	0.42 ± 0.35*
0.045	-	-	-	-	x	0.38 ± 0.41	0.10 ± 0.46	0.18 ± 0.50	0.10 ± 0.45	0.39 ± 0.53	0.34 ± 0.53
0.055	-	-	-	-	-	x	0.28 ± 0.39	0.20 ± 0.34	0.27 ± 0.46	0.04 ± 0.39	0.02 ± 0.44
0.065	-	-	-	-	-	-	x	0.08 ± 0.30	0.01 ± 0.53	0.31 ± 0.43	0.26 ± 0.33
0.075	-	-	-	-	-	-	-	x	0.18 ± 0.51	0.25 ± 0.41	0.20 ± 0.33
0.085	-	-	-	-	-	-	-	-	x	0.13 ± 0.41	0.08 ± 0.56
0.095	-	-	-	-	-	-	-	-	-	x	0.06 ± 0.44
0.105	-	-	-	-	-	-	-	-	-	-	x

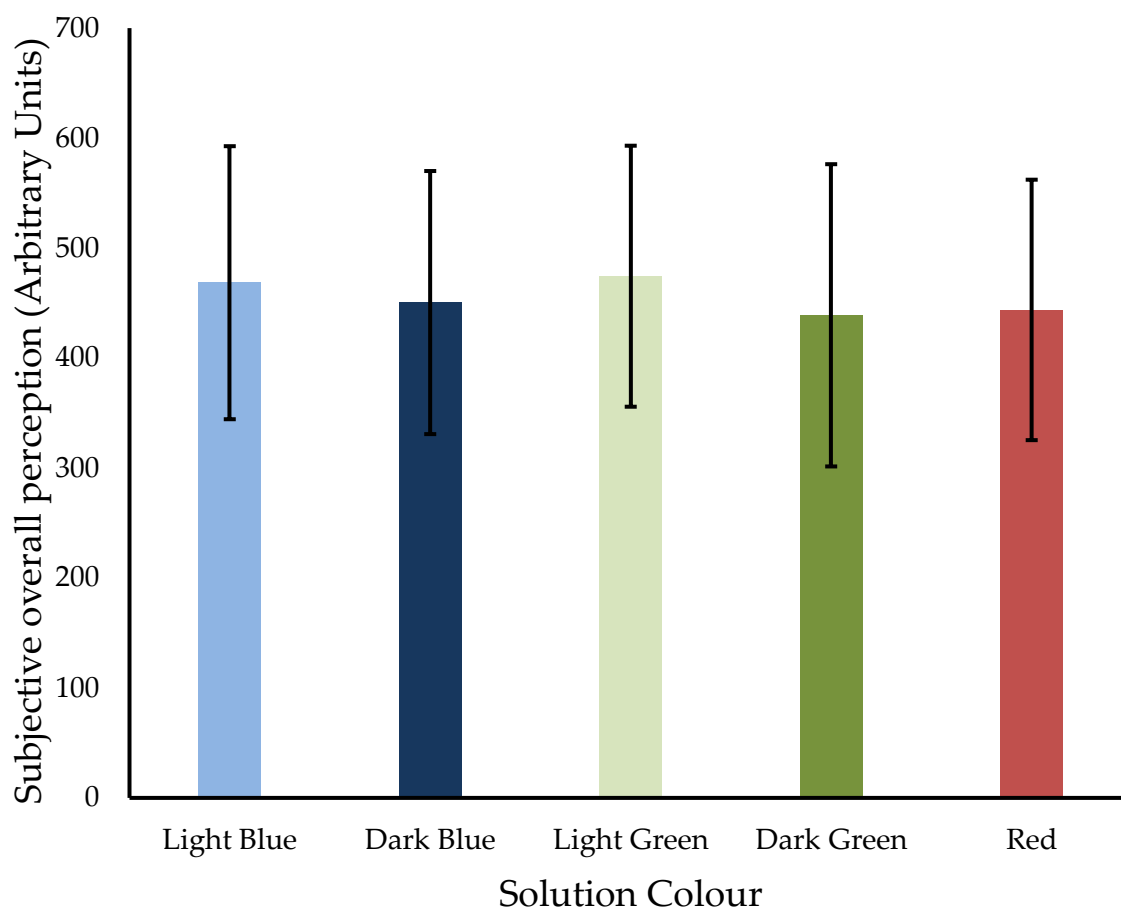


Figure 5-2 Subjective overall perception (Arbitrary Units) for solution colour, expressed as Mean VAS rating per solution colour \pm 1 S.D.

5.4 Discussion

Menthol mouth swilling is considered a practical ergogenic strategy before and during exercise in hot environments (Stevens, Taylor and Dascombe, 2016; Best *et al.*, 2018) and has been used to improve performance during time trials (Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016) and time to exhaustion (Mündel and Jones, 2009; Flood, Waldron and Jeffries, 2017). Perception of menthol mouth swill concentration may be highly individual in nature, with 200 gene variants of the receptor responsible for menthol detection (TRPM8 (Morgan, Sadofsky and Morice, 2015)). This may in part explain the broad standard deviations and confidence intervals overlapping zero in our results.

Perception may be dependent upon physiological factors such as trigeminal chemosensitivity (Frasnelli *et al.*, 2011; Michlig *et al.*, 2016) and stratum corneum thickness (H.R. Watson *et al.*, 1978), or environmental influences such as previous or habitual exposure to trigeminal agonists (Cliff and Green, 1996; Gillis *et al.*, 2015), e.g., regular use of mentholated products. Habitual menthol use may alter the threshold at which

TRPM8 channels and the trigeminal nerve are stimulated (Kalantzis, Robinson and Loescher, 2007; Klein *et al.*, 2010; Gillis *et al.*, 2015; Botonis *et al.*, 2016), ultimately habituating thermal sensation (Gillis *et al.*, 2015; Botonis *et al.*, 2016). Despite no statistically significant differences in the present investigation, menthol concentrations of 0.095–0.105% may lead to small increases in trigeminal stimulation, concomitantly conferring benefits such as an increase in ventilation (Mündel and Jones, 2009; Stevens and Best, 2017), reduced thermal sensation (Stevens, Thoseby, *et al.*, 2016) and thirst (Eccles *et al.*, 2013), and improved thermal comfort (Riera *et al.*, 2014) when exposed to the oral cavity.

The possibility that repeated menthol exposure may confer greater benefits than a single dose of menthol has not been directly explored to date. All menthol-containing studies (Mündel and Jones, 2009; Riera *et al.*, 2014; Tran Trong *et al.*, 2015; Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016; Riera *et al.*, 2016; Flood, Waldron and Jeffries, 2017) have employed a repeated exposure during the exercise bout—this is quantified via time or distance. Better understanding the time course of menthol mouth swilling responses, and the potential impact of concentrations upon these, would provide insight into possible limitations in application for menthol-containing strategies.

The highest rated solution colour in this investigation (Light Green; 474.40 ± 118.68 Arbitrary Units). The Light Blue solution was also rated highly, with trivial effects reported between Light Green and Light Blue (468.49 ± 124.15 Arbitrary Units; 0.05 ± 0.20 Trivial). Menthol-containing products such as mouth-wash, confectionary and other oral hygiene products are associated with these colours (Shankar, Levitan and Spence, 2010; Spence, 2015), and subjective qualities of solution may be enhanced due to this association (Michael and Rolhion, 2008; Fenko, Schifferstein and Hekkert, 2010; Yu *et al.*, 2017). In the absence of significant results between solution colours, researchers may consider using a light green or light blue coloured solution as a starting point for future menthol research.

The perception of colour and concentration may be influenced via the environment in which the solution is administered. The present study was conducted in an ambient temperature laboratory (22 ± 0.3 °C), which may have enhanced the subjective qualities of the menthol solution(s). For example, blue and green are typically associated with cooling (Michael and Rolhion, 2008; Fenko, Schifferstein and Hekkert, 2010), participants may have therefore perceived these colours as more refreshing than red, which is associated with warming (de Craen *et al.*, 1996; Fenko, Schifferstein and Hekkert, 2010). Future research should aim to understand the perception of concentration and colour under

differing environmental conditions; especially those conditions that are below 8 °C or exceed 28 °C. These temperatures represent threshold values for the menthol receptor TRMP8 (Patel, Ishiuchi and Yosipovitch, 2007), and the human thermoneutral zone (≥ 28 °C (Bligh and Johnson, 1973; Cabanac and Massonnet, 1977; Best, Payton *et al.*, 2018)). Investigations at the upper limit of, or exceeding this range are greater than the temperature at which the rate of metabolic heat production exceeds the rate of thermal transfer to the environment (25 °C (Kenny and Jay, 2013)). This provides an important platform from which to study the perceptual and physiological responses to menthol mouth swilling during exercise. The mode (e.g., running or cycling (Mora-Rodriguez, Ortega and Hamouti, 2011; Junge *et al.*, 2016)) and nature (continuous or interval; (Mora-Rodriguez, Del Coso and Estevez, 2008)) of exercise are also important experimental concerns, due to differences in heat production, heat storage, and hyperthermia risk (Mora-Rodriguez, Ortega and Hamouti, 2011).

Practically, the effect of colour extends beyond the aesthetic qualities of a solution or treatment; treatment colour may impart emotional modifications that could be tailored to an athlete's psychological profile. Red is typically associated with high arousal states (Dreiskaemper *et al.*, 2013; Briki and Hue, 2016), anger (Fetterman *et al.*, 2010) and danger (Young *et al.*, 2013); red has also been associated with Tae Kwondo match outcome (Falcó, Conchado and Estevan, 2016). Conversely, blue and green are perceived as calming (de Craen *et al.*, 1996), only slightly arousing (Briki and Hue, 2016), and in congruence with our findings have been shown to be perceived as more pleasant than red (Briki and Hue, 2016). Recently, a green inert drink was used to facilitate an induced beliefs investigation into sprint performance (la Vega *et al.*, 2017). The colour green was chosen specifically in this investigation due to the potency of belief around green substances' abilities to enhance performance (Szabo *et al.*, 2013; la Vega *et al.*, 2017). Such expectancy cannot be ignored in our investigation, or the practical application(s) of its findings. Furthermore, perceptions and preferences of colour, vary between individuals, within groups and across cultures (C. Taylor, Clifford and Franklin, 2013). Colours can be interpreted as having opposing meanings in different countries and cultures (Al-Rasheed, 2015), but in multi-cultural individuals have been reported to be interpreted intermediately (Yokosawa *et al.*, 2016), careful consideration of cultural perceptions would further enhance the implementation of our findings.

5.5 Conclusion

Based upon the results of our study, we recommend athletes and practitioners work together to ascertain a menthol concentration for mouth swilling. This concentration would ideally be based upon an individual's perception of the characteristics assessed in this work, and their competitive and training environment(s). Similarly, for practitioners, we advise using a light blue or green solution as a starting point for further investigation, given the synonymy with menthol containing products, but acknowledge that other cultural factors may influence this decision.

5.6 Addendum to Chapter 5: The Development of a Menthol Solution for use during Sport and Exercise

This addendum does not appear in the published version of this chapter (Best, Spears, *et al.*, 2018) but has been included at the request of examiners to further elucidate the values presented in Figure 5.1B, and thus proffer an explanation as to the influence of each of the assessed variables (Smell, Taste, Mouth Feel, Freshness and Irritation) upon the total score of each menthol solution concentration.

A forced entry multiple linear regression was performed in SPSS (v 26, IBM, New York, NY, USA). This methodology was used to counter the concerns regarding the stepwise approach, as outlined by Smith (2018). This regression model ranks contributing variables (Smell, Taste, Mouth Feel, Freshness and Irritation) by their ability to explain the change in total solution score. Between concentration comparisons via standardised mean differences were calculated made for the top weighted variable, and individual responses represented pictorially (Figure 5.3). Smallest worthwhile change (mm) was calculated as $0.2 \times$ between subjects' standard deviation for the variable(s) of interest, equating to 7.52mm.

5.6.1 Multiple Linear Regression

The model explained nearly all the variance in total solution score ($R^2 = 0.994$), and could significantly predict total solution score, $F(5, 220) = 7643.5$, $p < 0.001$. All variables significantly predicted total solution score (all $p < 0.001$), individual contributions to the model (b values), their standard errors and standardised values (β) are presented in table 5.2 below. Real change values (i.e. how many mm a change of one standard deviation of a variable contributes to total VAS score) are also included; real changes are calculated by multiplying the standard deviation of each variable by its standardised value (β).

Table 5-2 Results of Multiple Regression analysis; all variables are significant predictors at $p < 0.001$

Variable	b	SE b	β	Real change (mm)
Constant	1.561	2.176	-	-
Freshness	.942	0.022	.261	7.855
Smell	1.016	0.020	.278	8.288
Taste	0.977	0.020	.291	9.426
Mouth Feel	1.054	0.022	.315	10.241
Irritation	0.979	0.017	.347	13.371

Collinearity is the extent to which multiple predictor variables within the model, correlate with each other; clearly if this is shown to occur, it is problematic as multiple predictors may predict an overlapping amount of variance within the dependent variable, and thus explain similar or the same parts of the model. Collinearity between variables was assessed by examining the average (mean) of variance inflation factors (VIF) and tolerance statistics for each variable. Collinearity was defined as a mean VIF substantially greater than 1, and tolerance statistics <0.2 , as per Field (2011). Mean VIF was 1.411 and all tolerance statistics were >0.2 (0.584 – 0.847) so collinearity between variables was considered not to have occurred.

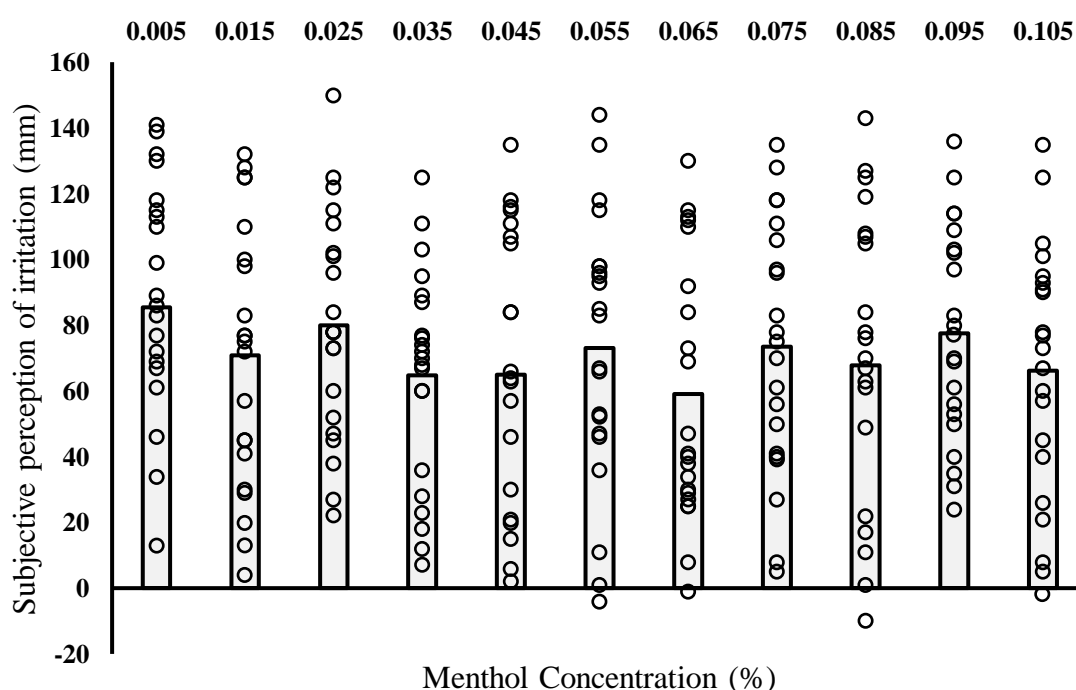


Figure 5-3 Individual and mean responses for perceptions of irritation, per concentration. Mean responses are represented by shaded bars, individual responses by open circles

Table 5-3 Effect Sizes and accompanying 90% Confidence Intervals for irritation. Effect Size thresholds are Trivial (>0.20) Small (0.2 - 0.6) Medium (0.6 – 1.2) Large (1.2 – 2.0) Very Large (>2.0) as per Hopkins (2010). Small effects with confidence intervals not zero are marked with an asterisk (*).

	0.005	0.015	0.025	0.035	0.045	0.055	0.065	0.075	0.085	0.095	0.105
0.005	X	0.43 ± 0.51	0.29 ± 0.48	0.62 ± 0.43*	0.56 ± 0.49*	0.32 ± 0.39	0.71 ± 0.37*	0.42 ± 0.50	0.59 ± 0.47*	0.25 ± 0.38	0.52 ± 0.50*
0.015	-	x	0.24 ± 0.29	0.16 ± 0.20	0.12 ± 0.28	0.06 ± 0.28	-0.29 ± 0.38	0.07 ± 0.35	0.08 ± 0.33	0.17 ± 0.39	-0.11 ± 0.33
0.025	-	-	x	-0.39 ± 0.30*	-0.31 ± 0.26*	-0.18 ± 0.40	-0.52 ± 0.44*	-0.16 ± 0.31	-0.14 ± 0.35	-0.06 ± 0.36	-0.35 ± 0.40
0.035	-	-	-	x	0.09 ± 0.30	0.21 ± 0.27	-0.14 ± 0.31	0.23 ± 0.28	0.22 ± 0.32	0.34 ± 0.35	0.04 ± 0.20
0.045	-	-	-	-	x	0.11 ± 0.37	-0.20 ± 0.42	0.10 ± 0.35	0.12 ± 0.38	0.19 ± 0.43	-0.09 ± 0.38
0.055	-	-	-	-	-	x	-0.33 ± 0.30*	0.01 ± 0.33	-0.06 ± 0.31	0.11 ± 0.30	-0.17 ± 0.36
0.065	-	-	-	-	-	-	x	0.36 ± 0.31*	0.24 ± 0.35	0.46 ± 0.36*	0.18 ± 0.32
0.075	-	-	-	-	-	-	-	x	-0.01 ± 0.36	0.10 ± 0.30	-0.18 ± 0.28
0.085	-	-	-	-	-	-	-	-	x	0.13 ± 0.35	-0.15 ± 0.35
0.095	-	-	-	-	-	-	-	-	-	x	-0.30 ± 0.36
0.105	-	-	-	-	-	-	-	-	-	-	x

5.6.2 Discussion

The model found that irritation accounted for the most real change (mm) in total solution score, suggesting that participants' sensory preferences may primarily be based upon their rating of a solution's irritation. This can be attributed, at least in part, to the wording of the polarised descriptors: "Unpleasant" and "Pleasant". A lower concentration of menthol is less likely to be interpreted as irritating due to the solution's higher water percentage, relative to higher concentration menthol solutions. Interestingly, these responses were neither unanimous nor dose dependent (i.e. progressively greater pleasant scores as menthol concentration decreased). The 0.005% solution differed by \geq SWC to all but one solution (0.025%), yet the distribution of the data (Figure 5.3) demonstrates participants do not consistently interpret menthol concentrations within this range as either pleasant or unpleasant. A larger sample size is required to elucidate any apparent trends in the figure, and a Likert scale as opposed to a VAS may have produced more discrete results due to a greater number of anchors and fewer possible responses, as opposed to the 150mm scale used in the present investigation.

Given its weighting in the multiple linear regression model, a similar interpretation is likely acceptable for mouth feel. The weighting of irritation and mouth feel within the model begs the question of whether participants are assessing the most pleasant solution or the least unpleasant? This is an important consideration for athletes and associated practitioners who are looking to employ the strategy of menthol mouth rinsing in the field. It may not matter whether the athlete enjoys the characteristics of the solution, more that these characteristics are sufficient so that they can be qualitatively accepted and tolerated by the athlete during their performance, and any beneficial performance effects manifested.

CHAPTER 6 : PERCEPTUAL AND PHYSIOLOGICAL RESPONSES TO CARBOHYDRATE AND MENTHOL MOUTH-SWILLING SOLUTIONS

Carbohydrate and menthol mouth-swilling have been used to enhance exercise performance in the heat. However, these strategies differ in mechanism and subjective experience. Participants (n=12) sat for 60 min in an environmental chamber (35°C; 15±2%), following a 15 min control period, participants undertook three 15 min testing blocks. A randomised swill (Carbohydrate; Menthol; Water) was administered per testing block (one swill every three minutes within each block). Heart rate, tympanic temperature, thermal comfort, thermal sensation and thirst were recorded every three minutes. Data were initially analysed by ANOVA with carbohydrate intake subsequently controlled for via ANCOVA. Data are reported as effect size \pm 90% confidence intervals, with accompanying descriptors. Small elevations in heart rate were observed after carbohydrate (ES: 0.22 \pm 90% CI: -0.09 to 0.52) and water (0.26; -0.04 to 0.54). Tympanic temperature was moderately different between control and all testing blocks. Menthol showed small improvements in thermal comfort relative to carbohydrate (-0.33; -0.63 to 0.03) and water (-0.40; -0.70 to -0.10), and induced moderate reductions in thermal sensation (-0.71; -1.01 to -0.40 and -0.66; -0.97 to -0.35, respectively). Menthol reduced thirst by a small to moderate extent. These effects persisted when controlling for carbohydrate intake: menthol improved thermal comfort compared to carbohydrate (0.29; -0.09 to 0.65) and water (0.41; 0.04 to 0.78), and elicited small to moderate improvements in thermal sensation (-0.63; -1.00 to -0.25 and -0.38; -0.75 to -0.01) and thirst (-0.46; -0.83 to -0.08 and -0.67; -1.04 to -0.29). Carbohydrate and water may elevate HR, whereas menthol elicits small improvements in thermal comfort, moderately improves thermal sensation and may mitigate thirst; these effects persist when dietary carbohydrate intake is controlled for.

6.1 Introduction

Mouth swilling is an increasingly popular ergogenic strategy employed by athletes over short to moderate exercise durations (Carter and Jeukendrup, 2004; Painelli, Nicastro and Lancha, 2010; Pottier *et al.*, 2010; Rollo and Williams, 2011; Burke and Maughan, 2014;

Peart, 2017), during nutrient restricted states (Fares and Kayser, 2011; S.C. Lane *et al.*, 2013; Che Muhamed *et al.*, 2014; Ataide-Silva *et al.*, 2016), and may be appropriate during times of potential gastrointestinal distress (de Oliveira, Burini and Jeukendrup, 2014; Stuempfle and Hoffman, 2015). Multiple nutritional stimuli are swilled, with each conferring a different ergogenic effect and magnitude thereof (Rollo and Williams, 2011; Beaven *et al.*, 2013; Burke and Maughan, 2014; Zhang *et al.*, 2014; Stevens and Best, 2017), most likely due to affecting differing sensory pathways. More precisely, as the nutritional stimulus being swilled changes the cells targeted by, and exposed to, the swill also alter and the resultant ergogenic effect is the product of these interactions. Nutritional stimuli that are swilled either directly or indirectly affect the brain and bypass the digestive system, thereby reducing energy intake and the risk of gastrointestinal distress, which is frequently reported during prolonged endurance activity (de Oliveira, Burini and Jeukendrup, 2014; Stuempfle and Hoffman, 2015; Costa *et al.*, 2016; 2017) when caffeine (Papakonstantinou *et al.*, 2016) and / or carbohydrate are ingested (Stuempfle, Hoffman and Hew-Butler, 2013; Stuempfle and Hoffman, 2015; Wardenaar *et al.*, 2015).

Carbohydrate (CHO) is considered the gold-standard ergogenic mouth swilling strategy, with a wealth of literature documenting its efficacy in contrasting environments (Cramer, Thompson and Périard, 2015), nutritional states (Fares and Kayser, 2011) and sports (Stellingwerff and Cox, 2014; Clarke, Kornilios and Richardson, 2015; Williams and Rollo, 2015). Mechanistically, CHO is shown to activate areas of the brain that are associated with behavioural, cognitive and emotional responses (Carter and Jeukendrup, 2004), with areas associated with motivation and motor control also stimulated (Gant, Stinear and Byblow, 2010). Activation of these higher order and efferent regions of the brain, as supported by fMRI, provide strong explanation(s) for CHO mouth swilling's ergogenic effects to date, but CHO is also shown to affect receptors within the oral cavity (Chambers, Bridge and Jones, 2009), as is caffeine (Devillier, Naline and Grassin-Delyle, 2015; Liszt *et al.*, 2017; Lipchok *et al.*, 2017) and menthol (Eccles, 1994; Eccles, Du-Plessis, Dommels and Wilkinson, 2013; Stevens and Best, 2017).

Menthol is considered a trigeminal afferent, stimulating the trigeminal nerve (Klein *et al.*, 2010; Frasnelli *et al.*, 2011) and associated TRPM8 receptors (Bautista *et al.*, 2007; Nazıroğlu and Özgül, 2011; Gavva *et al.*, 2012). The trigeminal network innervates the ophthalmic, mandibular and maxillary regions as shown below (*Figure 6.1*), with menthol and other cold stimuli particularly affecting the maxillary region, and due to its proximity to the nasal and oral cavities (Hummel and Livermore, 2002) stimuli have almost direct access to nerve endings due to the lack of squamous epithelia covering mucosa (Hummel and Livermore, 2002). Indeed, it is stimulation of this collection of nerves that is responsible for sphenopalatine ganglioneuralgia, or ‘brain freeze’ (Byrne *et al.*, 2011). This potent response highlights the sensitivity and role within cold temperature detection of TRPM8 receptors, and is likely enhanced due to the thinness of the membrane within the oral cavity (H.R. Watson *et al.*, 1978; Stevens and Best, 2017). Sports scientists have recently begun to investigate menthol mouth swilling as a strategy to ameliorate feelings of thermal comfort and sensation and exercise performance in hot conditions (Mündel and Jones, 2009; Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016; Flood, Waldron and Jeffries, 2017; Stevens and Best, 2017), but menthol may also confer hedonic and thirst attenuating responses that are yet to be investigated by sports scientists. These effects may in part be confounded by exercise due to effects such as increased ventilation

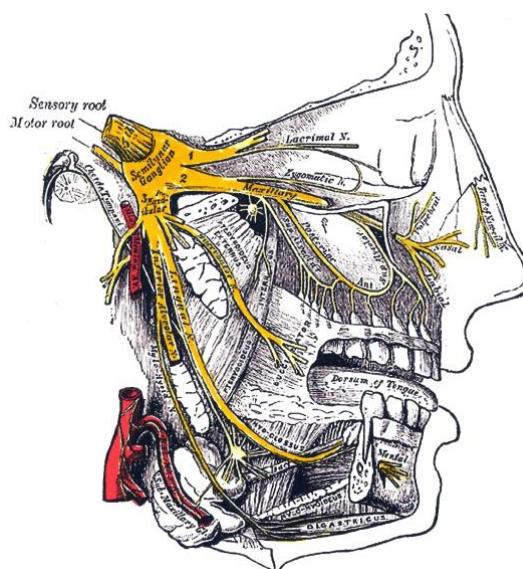


Figure 6-1 A classic anatomical drawing of the Trigeminal Nerve (Fig. 778; Grey). The nerve is depicted in yellow; the ophthalmic, maxillary and mandibular branches are numbered sequentially 1-3, respectively and emanate from the sphenopalatine ganglion.

(Meamarbashi and Rajabi, 2013; Best, Spears, *et al.*, 2018) and decreased salivary flow rate (Dawes, 1987), but may be enhanced in hot conditions due to menthol’s stimulatory effect upon TRPM8 receptors and the long-documented preference for application of cold

stimuli to the tongue and oral-cavity under thermally challenging circumstances (Eccles, 2000a; Eccles, Du-Plessis, Dommels and Wilkinson, 2013; Morris and Jay, 2016).

Assessment of the effect of differing mouth swilling strategies on physiological and subjective measures under resting conditions may further elucidate mechanistic differences between nutritional stimuli applied to the oral cavity, without confounding effects brought about by exercise. Therefore, the aim of this investigation was to quantify physiological and subjective responses to CHO and menthol mouth swilling at rest, under thermally challenging conditions.

6.2 Materials and Methods

This investigation employed a within subjects, repeated measures design with participant's baseline data serving as their reference values from which to derive experimental effects. Testing order of treatments within the experimental session was assigned via Latin square, using a customised spreadsheet (Pezzullo, 1999). All testing took place within an environmental chamber (Reltech, Gloucestershire, UK) set at 35°C and 10% humidity, with outcome measures assessed at three minute intervals. Participants completed the study with a single visit to the laboratory; comparisons for experimental effects are derived from within session and between time point comparisons for each swill, thus values are assessed for an effect of condition, time point, and an interaction between these variables. Nutritional intake was recorded via a 24-hour food recall preceding the experimental session. These data were used to calculate dietary carbohydrate intake using specialist software (Nutritics, version 5.0, 2018, Nutritics Limited, Dublin, Ireland) which was subsequently included as a covariate in multiple analysis of covariance (see 6.2.5), as carbohydrate intake has previously been shown to influence responses to carbohydrate mouth rinsing (Fares and Kayser, 2011). Participants were made aware of the aim, procedure and risks of the study prior to providing informed written consent. Ethical approval for this investigation was granted by the Teesside University School of Social Sciences, Business and Law ethics board.

6.2.1 Participants

Twelve participants (11 males and one post-menopausal female) took part in this investigation. Participants had a mean age of 31.45 years (\pm 90% CI: 26.88 to 36.02 years), and were 177.38 cm (172.99 cm to 181.76 cm) tall, weighing on average 75.87 kg (70.91 kg to 80.82 kg). Participants were non-heat acclimated and were screened for medical

issues that may have affected their ability to participate in the investigation prior to commencement.

6.2.2 Mouth swilling solutions

Solutions were prepared outside of the environmental chamber, under thermoneutral conditions (22 ± 0.5 °C), and administered in 25ml aliquots. Five swills took place per swill condition; swills lasted ~10 seconds prior to expectoration, with swilling order randomised via a Latin square design, using a customised spreadsheet (Pezzullo, 1999).

Menthol (MEN) was prepared to a 0.1% concentration, as per Chapter 5 (Best, Spears, *et al.*, 2018). Briefly, a 5% menthol ethanol-based stock solution was diluted to the desired concentration using distilled water. The carbohydrate mouth-swill (CHO) was prepared from unflavoured Maltodextrin (MyProtein, Northwich, United Kingdom), and was diluted to 10% concentration (100g.L^{-1}). Water acted as the placebo swill, and a control period of no swilling was incorporated into each testing session (see Procedure). Quasi-single blinding was employed, whereby solutions were matched to be colourless, but were not matched for taste.

6.2.3 Procedure

Testing began with 15 minutes of passive sitting, during which time outcome data were recorded by the researcher, but no swilling took place. Following this control period (CON), participants swilled their assigned swill at three minute intervals; five swills were completed per condition. Once the final swill was completed and outcome measures recorded, participants exited the chamber. The experimental procedure is pictorially represented in Figure 6.2.

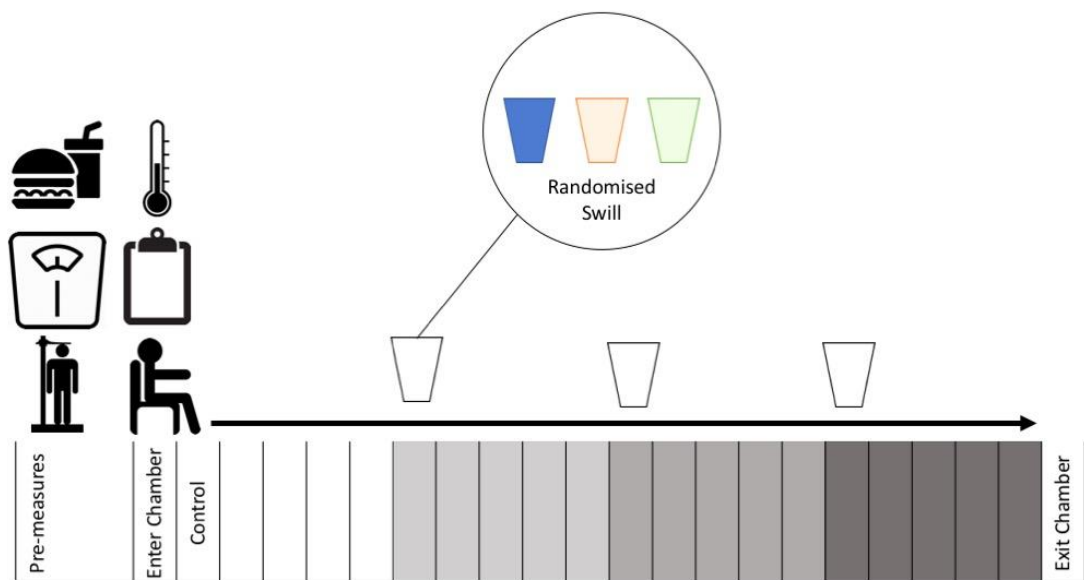


Figure 6-2 Experimental Procedure: Black vertical lines from entering the chamber represent three minute intervals; at each interval, physiological and subjective measures were assessed as indicated by the clipboard and thermometer. Blank vessels represent the commencement of a new randomised mouth swill; this is supported with a change in shade of time interval cells. Randomised swills included water (blue), carbohydrate (orange) and menthol (green).

6.2.4 Outcome Measures

6.2.4.1 Physiological measures

Tympanic temperature (T_{tym}) was assessed using a tympanic thermometer ($\pm 0.1^{\circ}\text{C}$), with measures taken from the ear contralateral to participants' dominant hand. Temperature was assessed prior to the administration of mouth swills, so any potential increase in temperature caused by swilling or local irritation would be mitigated. Heart rate (HR) values were recorded 10 seconds prior to each three-minute interval via telemetry (Polar RS400; Polar, Helsinki, Finland).

6.2.4.2 Subjective measures

Subjective measures were assessed using validated rating scales, with accompanying descriptors. Thirst was assessed via a 10-point scale (Appendix 3; (Engell *et al.*, 1987)), ranging from 'Not at all thirsty' to 'Extremely thirsty'. Zhang *et al.*'s scales of TC and TS were used to assess these qualities (Appendix 2 (Zhang *et al.*, 2004)). Both scales range from -4 to +4, with polar descriptors of Very Uncomfortable: Very Comfortable, and Very Cold: Very Hot, respectively. As a point of difference, the TC scale contains values of -0

and +0 to numerically describe just uncomfortable and just comfortable, respectively (Zhang *et al.*, 2004).

6.2.5 Statistical Analyses

Normality was assessed for using Skewness and Kurtosis tests (acceptable Z scores not exceeding +1 or -1). Initially, a two-way multiple analysis of variance (MANOVA) was conducted to determine differences between time and beverage type on physiological and subjective outcome measures. Secondly, a two-way multiple analysis of covariance (MANCOVA) was conducted to determine differences between time and beverage type on outcome measures when controlling for carbohydrate intake. Significance was set at an *a priori* alpha level of $p < 0.05$. Effect sizes are reported as standardised mean differences \pm 90% C.I., with accompanying descriptors (Hopkins *et al.*, 2009). Ninety percent (90%) C.I. are used to differentiate between any observed significant results and the likely range in which true differences may occur (Sterne and Smith, 2001; Hopkins *et al.*, 2009), as opposed to another method of expressing a significant result.

6.3 Results

6.3.1 Carbohydrate Intake

Mean carbohydrate intake for participants was 69.92g (\pm 90% CI: 55.89g to 83.94g), with an absolute range of 203g. These values are considered low in relation to participants' bodyweight (Thomas, Erdman and Burke, 2016), hence being stated in absolute as opposed to relative values.

6.3.2 MANOVA

There was a statistically significant interaction effect between time and mouth-swill type on combined dependent variables, $F(20,750.507) = 6.168$, $p < 0.0001$; Wilks' $\Lambda = 0.604$. This interaction effect is attributed to the significant effect of mouth-swill type on combined dependent variables, $F(10,452) = 2.419$, $p = 0.008$; Wilks' $\Lambda = 0.901$, whereas time demonstrated a non-significant effect on combined dependent variables, $F(10,452) = 1.090$, $p = 0.368$. Pairwise comparisons were used to identify significant effects upon dependent variables between mouth-swill types.

6.3.2.1 Physiological outcomes

Small (ES: 0.26; -0.04 to 0.54), significant differences in HR were observed between CON and water ($p = 0.018$). *Small* (0.22; -0.09 to 0.52) non-significant differences in HR were

also recorded between CON and CHO. All other HR comparisons were non-significant and trivial. Tympanic temperature during the CON period was significantly different to all other conditions (values; $p<0.001$), displaying *Moderate* effects (MEN: 0.89; 0.56 to 1.19. CHO: 0.91; 0.59 to 1.22. Water: 0.88; 0.56 to 1.19) Tympanic temperature displayed *Trivial*, non-significant effects across all other comparisons i.e. between swills.

6.3.2.2 Subjective outcomes

Thermal comfort was significantly greater ($p<0.002$) in CON compared to water swilling (*Small*; -0.39; -0.69 to -0.09). Despite not reaching statistical significance ($p<0.062$) there were *small* (-0.32; -0.63 to -0.02) differences in TC between CON and CHO conditions too, whereas MEN was only *trivially* different to CON (-0.01; -0.29 to 0.31). Menthol improved TC by a *small* magnitude compared to CHO (-0.33; -0.63 to -0.03) and water (-0.40; -0.70 to -0.10). Carbohydrate and water swilling were *trivially* different (0.10; -0.20 to 0.40) with respect to TC. Thermal sensation was *moderately* and significantly reduced by MEN in comparison to CON, CHO and water (see Table 6.1). All other comparisons were *trivially* and non-significantly different. Thirst was significantly greater in CON compared to MEN ($p<0.001$) and water ($p<0.011$), but not CHO ($p=0.134$); magnitudes of swilling's ability to improve thirst varied from *small* to *moderate* (see Table 1). Menthol lowered thirst significantly in comparison to CON and CHO, but not water; these differences were *moderate* in nature. Further contrasts are outlined in Table 1.

6.3.3 MANCOVA

Upon controlling for carbohydrate intake, there was a significant effect of mouth-swill type upon combined dependent variables $F(10,298) = 1.913$, $p<0.043$; Wilks' $\Lambda = 0.883$. Between subjects' comparisons revealed significant differences for TS ($p<0.004$) and thirst ($p<0.048$). Heart rate ($p<0.598$) and T_{tym} ($p<0.634$) responses were not significantly different between conditions when carbohydrate intake was controlled for, nor were differences in TC ($p<0.151$).

Despite non-significant differences in TC ($p<0.151$), when compared to both CHO (0.29; -0.09 to 0.65) and water (0.41; 0.04 to 0.78), MEN improved TC to a *small* extent. Pairwise comparisons demonstrated MEN significantly reduced TS in comparison to CHO (-0.36 units; $p<0.004$) and water (-0.37 units; $p<0.008$), exerting *moderate* (-0.63; -1.00 to -0.25) and *small* (-0.38; -0.75 to -0.01) effects respectively. Similar reductions in thirst were also observed, however in contrast to the unadjusted model MEN displayed a *moderate* (-0.67; -1.04 to -0.29) standardised mean difference in thirst compared to water of -0.69 units

($p < 0.023$), with a *small* (-0.46; -0.83 to -0.08) difference in comparison to CHO (-0.49 units; $p < 0.068$).

Table 6-1 Differences between mouth-swilling conditions for thermal sensation and thirst; significant effects are denoted by an asterisk (*) and emphasised in bold. ES: Effect Size; C.I.: Confidence Interval

Variable	Swill	Comparison	<i>p</i> value	ES; 90% C.I.	Descriptor
Thermal Sensation	Control	Menthol	0.001*	0.66; 0.34 to 0.96	Moderate
		Carbohydrate	0.835	0.04; -0.26 to 0.34	Trivial
		Water	0.878	0.06; -0.24 to 0.36	Trivial
	Menthol	Control	0.001*	-0.66; -0.96 to -0.34	Moderate
		Carbohydrate	0.001*	-0.71; -1.01 to -0.40	Moderate
		Water	0.001*	-0.66; -0.97 to -0.35	Moderate
	Carbohydrate	Control	0.835	-0.04; -0.34 to 0.26	Trivial
		Menthol	0.001*	0.71; 0.40 to 1.01	Moderate
		Water	0.965	0.02; -0.28 to 0.33	Trivial
	Water	Control	0.878	-0.06; -0.36 to 0.24	Trivial
		Menthol	0.001*	0.66; 0.35 to 0.97	Moderate
		Carbohydrate	0.965	-0.02; -0.33 to 0.28	Trivial
Thirst	Control	Menthol	0.001*	0.75; 0.43 to 1.06	Moderate
		Carbohydrate	0.134	0.26; -0.05 to 0.56	Small
		Water	0.011*	0.33; 0.02 to 0.63	Small
	Menthol	Control	0.001*	-0.75; -1.06 to -0.43	Moderate
		Carbohydrate	0.022*	-0.55; -0.85 to -0.24	Small
		Water	0.263	-0.49; -0.79 to 0.18	Small
	Carbohydrate	Control	0.134	0.26; -0.56 to 0.05	Small
		Menthol	0.022*	0.55; 0.24 to 0.85	Small
		Water	0.259	-0.07; -0.37 to 0.23	Trivial
	Water	Control	0.011*	-0.33; -0.02 to 0.44	Small
		Menthol	0.263	0.49; -0.18 to 0.79	Small
		Carbohydrate	0.259	0.07; -0.23 to 0.37	Trivial

6.4 Discussion

The aim of this study was to assess physiological and subjective responses to CHO and menthol mouth swilling, at rest under thermally challenging conditions, by employing a randomised tasting order in a quasi-blinded fashion.

Thermal Sensation was significantly improved, to a *moderate* degree by menthol in comparison to all other conditions. This finding has been reported repeatedly when menthol is applied to the oral cavity (Mündel and Jones, 2009; Stevens, Thoseby, *et al.*, 2016; Flood, Waldron and Jeffries, 2017), and topically by other researchers (Barwood, Corbett and White, 2014; Gillis *et al.*, 2016). However, we are the first group to document that this effect remains when nutrition (CHO intake) is accounted for statistically. This is important given the documented and potential use of menthol mouth swilling as an ergogenic aid during endurance exercise in thermally challenging conditions (Stevens, Thoseby, *et al.*, 2016; Stevens and Best, 2017; Best, Payton, *et al.*, 2018).

Further, this suggests that menthol mouth swilling has the potential to be incorporated alongside other nutritional practices that may not alter TS such as CHO intake during or following exercise. Such findings may be of use to athletes undertaking heat acclimation training, whereby the heat stimulus may be applied actively i.e. during exercise (Périard, Racinais and Sawka, 2015; Willmott *et al.*, 2016; Stevens, 2018), passively via hot-water immersion (Zurawlew *et al.*, 2016; Zurawlew, Mee and Walsh, 2018), or a sauna during recovery from exercise (Stanley *et al.*, 2014).

Alternatively, in competition this finding allows athletes to pursue complementary nutrition and thermal ergonomic strategies, potentially mitigating commonly reported issues during prolonged exercise (in the heat) such as gastrointestinal distress (Costa *et al.*, 2017; Costa, Hoffman and Stellingwerff, 2018) or taste fatigue (Costa, Hoffman and Stellingwerff, 2018). This finding also has relevance to armed or emergency service personnel, who may have to report rapidly to situations in thermally challenging environments, potentially in varying states of nutritional preparedness.

Thirst, on the other hand, may be a key indicator of physiological readiness in these professions, and in prolonged endurance activity may also convey homeostatic information. Menthol mouth rinsing likely satiates thirst via a pre-absorptive pathway (Eccles, Du-Plessis, Dommels and Wilkinson, 2013) through stimulation of oral cold receptors (Eccles, 2000b; Eccles, Du-Plessis, Dommels and Wilkinson, 2013), concomitantly conferring an hedonic effect, effectively mimicking a cold beverage. The hedonic relationship between beverage temperature is well described in humans (Brunstrom and Macrae, 1997; Mündel *et al.*, 2006; Burdon *et al.*, 2012), and has been

shown to occur in rodents even in the absence of thirst or water deficit (Torregrossa *et al.*, 2011). Therefore, when implementing mouth-swilling protocols, menthol's ability to attenuate thirst significantly, to a *small* to *moderate* extent, is something practitioners and scientists must consider. It is not clear from this investigation whether a brief application of menthol in a mouth-swill can alter exercise or thermoregulatory behaviours to the extent that they become detrimental to the individual in question. It would be prudent to recommend that menthol mouth-swilling be employed in compensable heat stress, in exercise durations whereby muscle glycogen concentration is not also a limiting factor, so reducing the need for further nutritional support e.g. events lasting ~60 min, or sports divided into periods of play. If athletes and practitioners still wish to employ menthol mouth-swilling in events outside of these constraints, then the co-implementation of other pre, or per-cooling strategies may be warranted (Bongers *et al.*, 2014; Stevens *et al.*, 2017; Best, Payton, *et al.*, 2018), and these should be accompanied by athlete or user education strategies from the supporting practitioner(s).

Thermal Comfort was also improved to a *small* extent by menthol mouth swilling when compared to CHO (-0.33; -0.63 to -0.03) and water (-0.40; -0.70 to -0.10). Conversely, menthol was *trivially* different to CON, displaying a broader confidence interval than for TS. Thermal comfort may be susceptible to a time effect in this investigation despite the randomised swilling order, as evidenced by participants reporting that CON was more thermally comfortable to a *small* extent, in comparison to CHO ($p < 0.062$) and water ($p < 0.002$) swills. As time progressed, participants may have experienced greater awareness of tactile elements of their environment such as the wettedness of clothing, local skin wettedness or the texture of the chair on which they were sat, as longer exposure to a hot environment elicits and accumulates a greater volume of sweat, through which a participant must interact with their tactile environment. Incorporating local measures of TC and skin wettedness in subsequent investigations would allow for greater precision in this hypothesis.

Heart rate and T_{tym} behaved differently over the course of the investigation. This is somewhat counterintuitive as typically we would expect a concomitant increase in both metrics over time, but not necessarily in response to swills. The expected time course response would be attributed to progressive heat load (Périard, Racinais and Sawka, 2015; Périard *et al.*, 2016), yet in the present investigation each swill appeared to produce a different response. When compared to the CON period, both water and CHO elicited *small* increases in HR, whereas menthol did not.

With respect to menthol, our findings are in keeping with those of Shepherd and Peart (2017) who rebutted the results of Meamarbashi and Rajabi (2013), who asserted that 10 days of supplementation with a peppermint oil solution has a stimulatory effect, increasing maximal HR achieved during a maximal exercise test by 8%, and also increasing a complement of other exercise associated variables. The *small* increases in HR observed during water and CHO swilling appear counterintuitive from a sport and exercise scientist's perspective, as an increase in HR would confer a cost to the athlete, especially in a hot environment, where factors such as increased sweat rate, resultant dehydration and increased skin blood flow already add to the thermal physiological strain experienced by the athlete (Racinais *et al.*, 2015). Yet at rest when paired with a pleasant stimulus, these responses are perfectly normal (Leterme *et al.*, 2008; Verastegui-Tena, van Trijp and Piqueras-Fiszman, 2018). Indeed, these responses have been noted to be goal directed (Richter and Gendolla, 2009; Brinkmann and Franzen, 2013), and increases in HR are associated with expectancy (Verastegui-Tena, van Trijp and Piqueras-Fiszman, 2018), and a higher perceived reward value in healthy individuals (Richter and Gendolla, 2009; Brinkmann and Franzen, 2013). Carbohydrate and water both confer hedonic responses by stimulating either receptors associated with fuel availability (Burke and Maughan, 2014), or oral cold receptors respectively (Eccles, Du-Plessis, Dommels and Wilkinson, 2013), and may convey a homeostatically derived sense of reward; thus an elevation in HR is probable. An alternative explanation for the elevation in HR in the present study is that of habituation (Verastegui-Tena, van Trijp and Piqueras-Fiszman, 2018). Heart rate responses have been shown to be greater in response to an habituated 15.4% sucrose solution in comparison to water (control) or quinine solution (bitter); this response is consistent between exposures and independent of participant expectation (Verastegui-Tena, van Trijp and Piqueras-Fiszman, 2018). Menthol mouth swilling on the other hand may be too novel a stimulus for participants to be habituated to and subsequently elicit a HR response, but its ability to be of hedonic value in the current investigation is evidenced by improvements in TC and TS. Habituation to menthol mouth swilling requires further investigation; frequent users of oral hygiene products may present a logical starting population.

To conclude, menthol mouth swilling improves perceptions of TC and TS, and satiates thirst compared to mouth swilling with other solutions. Carbohydrate intake can alter the perceptual characteristics of other swills, and thus the nutritional state of those undertaking mouth swilling strategies is a key consideration for supporting practitioners and users. Swilling carbohydrate and water may lead to *small* elevations in HR, and this may be an

anticipatory and / or habituated hedonic response. Menthol mouth swilling only *trivially* affects HR, but habituation to menthol mouth swilling warrants further exploration.

Chapter 7 : MENTHOL MOUTH SWILLING AND RUNNING PERFORMANCE AT DIFFERENT INTENSITIES AND TEMPERATURES⁴

Menthol is used to evoke pleasant feelings of coolness and freshness. Sports science has focused upon the topical or oral application of menthol to athletes, either directly on the skin or menthol soaked garments, and as a mouth rinse or in beverages. Interest has largely been in endurance activity, with increased time to exhaustion and time trial performance shown. Participants are also typically of limited or recreational fitness, therefore we recorded the perceptual responses to menthol mouth rinsing in trained endurance runners, at typical training and racing intensities. Seven runners (5km PB: 15:24 ± 00:39) completed a modified running economy test (14 – 20km.h⁻¹) and 1km time trial in 15°C and 28°C, with (+M) and without menthol. Physiological variables ($\dot{V}O_2$, $\dot{V}E$, HR, [La]) and accompanying differential ratings of perceived exertion were assessed. Thirst, Thermal Comfort (TC) and Thermal Sensation (TS) were also recorded.

Respiratory measures ($\dot{V}O_2$ and $\dot{V}E$) showed predominantly unclear responses throughout the running economy test and 1km time trial, however $\dot{V}E$ tended to increase following menthol use in 28°C. Large reductions in RPE_{over} were noted post time trial in 28°C+M, but this may be explained by a more conservative pacing strategy. Unclear responses for TS were found within temperatures, but increased between temperatures. Thirst and TC responses were unclear within temperatures, but thirst was elevated at higher speeds between temperatures. Finally, TC was improved at 16 and 18km.h⁻¹ in 15°C+M. These varied responses suggest either an individual tolerance to menthol, or that trained athletes are less susceptible to the perceptual thermal challenges of exercise, than previously studied lesser trained populations.

7.1 Introduction

To date, menthol mouth swilling work in runners has been confined to time trial models (Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016), and this model has also been used to assess topical application of menthol (Barwood, Corbett and White, 2014). These studies have also limited their athletes to 5km time trial simulations. Whilst a good

⁴ This work was funded by the British Milers Club Frank Horwill Scholarship 2016. This work was presented in part at the Sport and Exercise New Zealand Conference 2017.

representation of the competitive demands of running competition, especially in the work of Stevens, who used a non-motorised treadmill (Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016), athletes may also utilise nutritional strategies in training sessions (Stellingwerff, Boit and Res, 2007; Thomas, Erdman and Burke, 2016; Costa *et al.*, 2017), and are encouraged to do so in preparation for competitive events (de Oliveira, Burini and Jeukendrup, 2014; Jeukendrup, 2014). The only work to date that has assessed oral menthol application in a simulated training session is that of Tran Trong and colleagues (Tran Trong *et al.*, 2015) during a simulated ‘brick session’, consisting of three blocks of 4km cycling and 1.5km running, in trained triathletes ($\dot{V}O_{2\max}$ $59 \pm 11 \text{ ml} \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$). An experimental design that considers both training and racing velocities in trained runners is required to extend the knowledge pool beyond self-paced time trials, and potentially ascertain if menthol mouth-swilling demonstrates greater effects on pertinent physiological, subjective and ventilatory variables at typical training or racing paces.

Running economy (RE) assessments identify the cost of running at a given speed. Such tests have been shown to be reliable with a low coefficient of variation in well-trained athletes (Saunders, Pyne, Telford and Hawley, 2004b), and normative values are available across a range of paces (Barnes and Kilding, 2015). Sixteen kilometres per hour is often the speed at which RE assessments take place, given its submaximal intensity in well-trained runners (A. M. Jones, 2006). Saunders improved upon this by developing a multi-stage assessment, consisting of three four-minute stages at submaximal intensities of 14, 16 and $18 \text{ km} \cdot \text{h}^{-1}$ (Saunders, Pyne, Telford and Hawley, 2004b). A multi-stage model allows for deeper understanding of the cost of typical training intensities within and between athletes, but is representative of neither the competitive demands nor the physiological intensities of racing.

Running economy is typically expressed as the oxygen cost ($\dot{V}O_2$) required to run at a given speed, which is then tracked over time within athletes (A. M. Jones, 1998; 2006), and between athletes and paces (Saunders, Pyne, Telford and Hawley, 2004b; Millet, Hoffman and Morin, 2012; Hoogkamer *et al.*, 2016). However, suggestions that a more appropriate expression of running economy may be to describe running economy per unit of distance covered ($\text{L} \cdot \text{km}^{-1}$ and $\text{ml} \cdot \text{km}^{-1} \cdot \text{kg}^{-1}$), or as an energetic cost over time ($\text{kcal} \cdot \text{min}^{-1}$) or distance ($\text{kcal} \cdot \text{km}^{-1}$), have also been made (Foster and Lucia, 2007; Fletcher, Esau and MacIntosh, 2009; Shaw *et al.*, 2013; Barnes and Kilding, 2015; Shaw *et al.*, 2015). Irrespective of how it is expressed, RE is considered a key differentiator between athletes of similar aerobic capabilities i.e. $\dot{V}O_{2\max}$ (Bassett and Howley, 1997; 2000; Saunders, Pyne, Telford and Hawley, 2004b; Joyner and Coyle, 2008; Barnes and Kilding, 2015).

Further support for RE's position as a key performance determinant comes from case studies of champion athletes who demonstrate exceptional RE values (A. M. Jones, 1998; 2006; Lucia *et al.*, 2008). These values are typically exhibited in long-distance as opposed to middle-distance runners (Sjödén and Svedenhag, 1985; J. Daniels and N. Daniels, 1992; Barnes and Kilding, 2015). It is hypothesised that improved RE is accrued over time, resulting from chronic training volumes (Scrimgeour *et al.*, 1986), but RE is also influenced by anthropometric (Saunders, Pyne, Telford and Hawley, 2004a; Lucia *et al.*, 2006; Barnes and Kilding, 2015; Dervis *et al.*, 2016), biomechanical (Saunders, Pyne, Telford and Hawley, 2004a; Foster and Lucia, 2007; Rogers *et al.*, 2017; Marcello, B. K. Greer and A. E. Greer, 2017), and environmental factors (Maughan, 2010; Ely *et al.*, 2010; Junge *et al.*, 2016). Running economy is also postulated to have a genetic component, despite an absence of clear evidence (Scott and Pitsiladis, 2007; Joyner and Coyle, 2008). As RE is multifaceted, it follows that interventions have attempted to target differing contributing systems. Most recently, novel footwear technologies have been shown to induce improvements in RE (Hoogkamer *et al.*, 2017). Tried and tested methods such as strength training (Paavolainen *et al.*, 1999; Saunders, Pyne, Telford and Hawley, 2004a; Barnes and Kilding, 2015) and plyometrics (Dumke *et al.*, 2010) have also been shown to promote improvements in RE. These methods focus primarily on biomechanical and physiological alterations within the lower leg musculature, increasing elastic storage and energetic application and return through the ground (Foster and Lucia, 2007; Barnes and Kilding, 2015; Rogers *et al.*, 2017). Nutritionally, carbohydrate (Rapoport, 2010; Stellingwerff and Cox, 2014; Jeukendrup, 2014; Stellingwerff, 2016), and dietary nitrate (A. M. Jones, 2014; Pawlak-Chaouch *et al.*, 2016) have been shown to positively influence the oxygen cost of running, whereas dietary fat intake adversely affects exercise economy (Burke, 2015; Volek *et al.*, 2016; Burke *et al.*, 2017). If menthol mouth-swilling is to be considered a potential adjunct to runners' performance nutrition strategies, its effects upon physiological variables, namely RE, should be assessed at a range of speeds associated with training and racing in differing environmental conditions. Hence, the aim of this study was to investigate the effects of menthol mouth swilling upon physiological and perceptual variables at differing speeds and temperatures, representative of British training and competitive environments.

Table 7-1 References values for $\dot{V}O_{2\max}$, based upon competitive level of athlete, adapted from Jones (2007; p152). Relative values are shown as opposed to absolute, as this is preferred when describing runners.

Level		$\dot{V}O_{2\max}$				
World class	Male	80	-	90	ml.kg ⁻¹ .min ⁻¹	
International	Male	70	-	80	ml.kg ⁻¹ .min ⁻¹	
National	Male	65	-	75	ml.kg ⁻¹ .min ⁻¹	
Junior National	Male	60	-	70	ml.kg ⁻¹ .min ⁻¹	

7.2 Materials and Methods

This study employed a post-only crossover design, in which participants served as their own controls. Experimental effects were derived from between condition comparisons and individual responses to each condition over time. Ethical approval for this investigation was granted by the Teesside University School of Social Sciences, Business and Law ethics board.

Prior to study commencement, participants completed a modified running economy test (Saunders *et al.*, 2004b) to establish $\dot{V}O_{2\max}$, and familiarise participants with blood lactate ([La]) sampling and reporting of dRPE values, using the CR100 scale (E. Borg and G. Borg, 2002). This session also served to familiarise participants with the experimental warm-up procedure and testing environment.

Nutritional intake was recorded via a 24-hour food recall preceding the first experimental session, with participants encouraged to consume a typical diet throughout the testing period. The 24-hour recall served as a template that participants aimed to replicate throughout the testing period, with a view to increasing experimental and ecological validity. Experimental sessions comprised four laboratory visits (one visit per condition: 14°C and 28°C, with and without menthol mouth swilling), with trial order assigned via a Latin square design, as per a customised spreadsheet (Pezzullo, 1999). All experimental sessions took place in an environmental chamber, with participants wearing a harness in case of involuntary collapse when exercising. Humidity was fixed at 10% and wind speed at 0 m.s⁻¹ to mitigate cooling or heat storage effects driven by environmental factors beyond temperature. Water was available *ad-libitum* at room temperature during exercise.

7.2.1 Participants

Seven male athletes took part in this investigation; participant information is presented below (Table 7.2). Participant attrition was low, but due to other racing commitments and

injury only 4 of the 7 participants provided a complete data set for all trials. Injury was not brought about by participation in this study. Testing sessions were incorporated into the participants' training schedule by their coach and would replace a weekly interval session. Training volume was requested to be maintained throughout the testing battery so results would be indicative of each athlete's typical abilities, and not the product of an increase or reduction in training volume. Athletes were requested to wear their preferred light training clothing e.g. shorts and singlet and racing flats to increase ecological validity. Nutritional intake was recorded prior to the first testing session via 24-hour recall, and participants were encouraged to consume a typical diet throughout the testing procedure. The 24-hour recall served as a template that participants aimed to replicate throughout their involvement in the testing, so dietary preparations were representative of habitual nutrition intake.

Table 7-2 Participant Anthropometric, Performance, Physiological and Training Characteristics

Participant	Height (cm)	Weight (kg)	Age (y)	5km P.B. (mm:ss)
1 SG	177.0	64.0	18.9	16:28
2 HBT	170.0	58.0	17.1	15:43
3 HA	175.0	66.4	18.1	15:46
4 DN	175.0	56.0	20.8	15:37
5 DS	183.0	67.9	27.9	14:20
6 RB	178.0	73.1	26.3	14:27
7 LGT	172.0	55.9	29.3	15:06
Mean \pm SD	175.7 \pm 3.9	63.0 \pm 6.1	22.6 \pm 4.7	15:21 \pm 00:43

7.2.2 Modified running economy test

Before undertaking any recorded exercise, participants completed a fixed warm up of 10-minutes at 10km.h⁻¹ on the same make and model of treadmill they would perform the running economy test on (h/p/cosmos Pulsar; h/p/cosmos Sports & Medical GMBH; Nussdorf-Traunstein, Germany).

Given the trained nature of the participants, and their typical race velocities, a modified version of Saunders *et al* (2004b) running economy test was designed to assess the effect of temperature and mouth swill upon running economy, and associated variables (see Outcome measures). A similar adaptation to match athletes' characteristics has been documented in the literature (Lucia *et al.*, 2006; Lucia *et al.*, 2008). The test consists of

the athlete completing 4-minute stages interspersed with 1-minute recoveries at increasing intensities. Saunders' protocol consists of three stages of 14, 16 and 18 km.h⁻¹ (Saunders *et al.*, 2004b). Our modified version of the protocol included a 20km.h⁻¹ stage, as this is representative of 5km or 10km race speed(s), depending upon the athlete in question (Table 7.2), and so is a pertinent speed to the sample. Participants then undertook their final 1-minute recovery before completing a 1km time trial. Respiratory measures were taken throughout the final two minutes of each stage (see Outcome measures), blood lactate [La] values were obtained from a sample taken from the non-dominant ring finger and analysed subsequently (YSI 2700 Select, YSI (UK) Ltd., Hampshire, United Kingdom). Heart rate (HR) values were recorded 30 seconds prior to stage completion using telemetry (Polar RS400; Polar, Helsinki, Finland). Subjective measures and tympanic temperature were recorded immediately following the completion of the stage. If swilling was required, this too would be completed during recovery. Participants would ingest 25ml of 0.1% menthol mouth swill and swill for 10-seconds before expectorating the solution and readying themselves for commencement of the next stage. Solution was provided in 25ml plastic containers, on a table in the environmental chamber that was positioned to mimic that of a feeding station in a race (waist height and at the runners' side). Participants were provided with a larger (250ml) cup for expectorated solution.

7.2.3 1km time trial

Participants completed the 20km.h⁻¹ stage and 1-minute recovery. The treadmill belt speed was maintained at 20km.h⁻¹, distance was monitored via linked software (Polar, Helsinki, Finland). Participants then resumed running and signalled to the researcher to increase, decrease or maintain treadmill belt speed, using hand gestures. A 'thumbs up' position was held to increase belt speed, a 'thumbs down' signal was used to signal a decrease in speed; speed was adjusted in 0.1km.h⁻¹ increments. Speed was maintained if no hand signal was used. Treadmill speed and heart rate were recorded at 30-second intervals throughout the time trial. Time to complete the 1km was timed using a stopwatch. Respiratory measures were taken throughout the entire time trial, blood lactate values, subjective measures and tympanic temperature were recorded upon completion of the time trial. Verbal encouragement was provided by the researcher throughout the trial to mimic a race environment and encourage a maximal effort. Feedback was provided on distance remaining in 200m intervals to replicate the feedback an athlete would obtain when running on a 400m athletics track e.g. 'One lap to go! Come on!'. No time constraints were imposed upon the athletes to complete the time trial. Upon completion of the 1km time

trial and associated measures, participants were escorted from the chamber and completed a 10-minute cool down at 10km.h⁻¹ on the same treadmill that they had warmed up on.

7.2.4 Conditions

Warm-up and cool down running took place outside of the environmental chamber in ambient laboratory conditions. All testing took place in an environmental chamber, with participants wearing a harness in case of involuntary collapse when exercising maximally. Environmental conditions were selected to mimic British/European racing temperatures whilst maximising heat storage responses during Hot trials. Cold trials were conducted in 14°C and Hot trials were conducted in 28°C. For all trials humidity was fixed at 10% and wind speed at 0 m.s⁻¹ to mitigate cooling effects driven by environmental factors beyond temperature and to maximise rates of heat storage. Menthol mouth swilling was administered during recoveries for Hot+M and Cold+M conditions. Water was available *ad-libitum* during recoveries and post-exercise.

7.2.5 Outcome measures

7.2.5.1 Physiological measures

$\dot{V}O_2$ (ml.min⁻¹ and ml.kg⁻¹.min⁻¹) and VE (L.min⁻¹) were assessed using breath by breath analysis (Piston HD6000, nSpire, nSpire Health Inc, Hertford, UK) for the final two minutes of each stage. Respiratory data was collected for the entire 1km time trial. Breath by breath $\dot{V}O_2$ was averaged for each stage. From this data was filtered using conditional formatting to obtain 30 seconds of data that was ± 50 ml from the mean. This method was chosen as steady state oxygen consumption has previously been defined as an increase of >100ml O₂ over the final two minutes of the stage (Fletcher, Esau and MacIntosh, 2009). For the 1km time trial section of the test peak $\dot{V}O_2$ ($\dot{V}O_{2peak}$) and VE values were recorded, as this better reflects the maximal demands of the activity than a mean value due to individual variation in $\dot{V}O_2$ kinetics and absence of a steady state during the time trials. Samples to be analysed for [La] were obtained from the non-dominant ring-finger using a lancet and collected in a capillary tube for automated analysis by a YSI 2700 Select analyser (YSI (UK) Ltd., Hampshire, United Kingdom) via a 25 µL sample and immediately analysed.

Temperature was recorded prior to the test session, and upon completion of each stage. Temperature was assessed using a tympanic thermometer ($\pm 0.1^\circ\text{C}$; Braun Thermoscan 5; Braun, Braun GmbH, Kronberg, Germany) and disposable caps, with measures taken from

the left ear. Temperature was assessed prior to the administration of the menthol, so any potential increase in temperature caused by swilling or local irritation would be mitigated.

7.2.5.2 Subjective measures

Subjective measures were assessed using validated rating scales, with accompanying descriptors. Thirst was assessed via Engell's scale (Appendix 3; (Engell *et al.*, 1987), ranging from 'Not at all thirsty' to 'Extremely thirsty'. Zhang *et al.*'s scales of thermal comfort (TC) and thermal sensation (TS) were used to assess these qualities (Appendix 2 (Zhang *et al.*, 2004). Both scales range from -4 to +4, with polar descriptors of Very Uncomfortable: Very Comfortable, and Very Cold: Very Hot, respectively. As a point of difference, the TC scale contains values of -0 and +0 to numerically describe just uncomfortable and just comfortable, respectively (Zhang *et al.*, 2004). Borg's CR100 scale (E. Borg and G. Borg, 2002) with idiomatic English verbal descriptors (Appendix 1) was used to assess dRPE. This differential approach assessed RPE at the legs (RPE_{legs}), lungs (RPE_{lungs}) and overall (RPE_{over}).

7.2.5.3 Time Trial Performance

Time trial performance was quantified as the time taken to complete 1km. Mean running speed was calculated upon completion, as the mean of the speeds recorded at 30 second intervals throughout. These speeds were also plotted per athlete, per condition to visualise pacing strategies.

7.2.4 Statistical Analyses

Data were analysed using standardised mean differences, via a customised spreadsheet (Hopkins, 2006). Magnitudes of effects were based upon standardised thresholds for *Small* (0.2), *Moderate* (0.6), *Large* (1.2) and *Very Large* (2.0) changes of standard deviations (Hopkins, Marshall, Batterham and Hanin, 2009), irrespective of outcome measure. Raw data are presented as mean \pm SD. Standardised mean differences are presented as effect sizes (ES) \pm 90% confidence intervals (C.I.).

Due to not meeting the demands of the testing sessions, as evidenced by performance outcomes and the ability of this data to notably alter the group mean(s), Participant 1 presented as a strong outlier, but did undertake all testing conditions. For this reason, data for 1km time trial are presented with and without Participant 1.

7.3 Results

Effect statistics for all dependent variables are presented in Tables 7.3 and 7.4 (ES \pm 90% C.I.) per stage and by condition interactions e.g. Cold vs. Hot. Confidence intervals that do not overlap zero are denoted by an asterisk.

7.3.1 Physiological Measures

7.3.1.1 Respiratory measures

When respiratory measures between Cold and Cold+M conditions were compared, differences across all speeds for $\dot{V}E$ and $\dot{V}O_2$ were unclear, except for a *small* increase (ES: $0.4 \pm 90\%$ CI: 0.34) in $\dot{V}E$ at 16km.h⁻¹. $\dot{V}O_2$ presented unclear differences across all speeds when Hot and Hot+M conditions were compared, whereas, $\dot{V}E$ trended towards an increase at all speeds, but standard deviations and confidence intervals overlapped zero (Table 7.2).

Between temperatures (Cold vs. Hot), there was an inverse relationship between differences in $\dot{V}E$ and running speed (Table 7.2), ranging from *Moderate* to *Small* in magnitude. This trend was not apparent between temperatures for $\dot{V}O_2$. Between mentholated conditions, Cold+M and Hot+M, similar differences in $\dot{V}E$ were observed, but confidence intervals overlap zero suggesting a less consistent effect because of menthol mouth-swilling. Differences between $\dot{V}O_2$ are similarly inconsistent, but trend towards a reduction in the heat as speed increases. However, these differences present with relatively broad standard deviations (Raw difference: -0.5 ± 3.2 to -3.7 ± 8.4 ml.kg⁻¹.min⁻¹). Effects upon $\dot{V}E$ and $\dot{V}O_2$ were all unclear, at all speeds in the remaining comparisons, with $\dot{V}E$ effects showing greater variability (Table 7.2).

During the time trial component (Table 7.3) $\dot{V}O_{2peak}$ was not affected by temperature nor menthol mouth-swilling; $\dot{V}E$ however, differed between temperatures by a *Small* to *Moderate* extent with lower $\dot{V}E$ values observed in hot conditions, but $\dot{V}E$ was not affected by menthol mouth-swilling.

7.3.1.2 Heart Rate, Lactate and Tympanic temperature

Heart rate increased following menthol mouth swilling in cold conditions (Cold+M), with the most notable and consistent difference occurring during the 1km time trial (*Small*; 0.54 ± 0.5). Similar trends were seen in hot conditions (Hot vs Hot+M) at lower speeds (14 and 16km.h⁻¹), but this effect diminished as running speed increased. HR was elevated in the heat, relative to cold condition (Cold vs. Hot), with the most pronounced difference occurring at 16 km.h⁻¹ (*Large*; 1.65 ± 0.53), and decreasing in magnitude as running speed

increased (*Moderate* to *Trivial*). There was no clear trend when comparing mentholated conditions (Cold+M vs. Hot+M). Remaining comparisons also demonstrate non-uniform effects, that may be driven either by menthol mouth-swilling or an elevated HR due to heat exposure.

Menthol mouth swilling led to a progressive increase in T_{tym} in cold conditions (Cold vs. Cold+M). Differences in T_{tym} showed a progressive, near linear increase in magnitude as speed increased from pre-test (-0.16 ± 0.5 ; *Trivial*), to 1km time trial completion (1.01 ± 0.58 ; *Large*). Conversely, there is an absence of such a trend between Hot and Hot+M conditions. *Small* reductions in T_{tym} are seen prior to the test commencing (-0.22 ± 0.18), and upon time trial completion (-0.56 ± 0.38), but all other speeds were trivially different between Hot conditions.

Between temperatures (Cold vs. Hot) *Large* to *Very Large* differences in T_{tym} were found across all speeds. When menthol-swilling conditions (Cold+M vs. Hot+M) were compared, T_{tym} is elevated across the testing bout (0.7 to 1.4°C), but effects show broader confidence intervals (Table 7.2). Remaining comparisons support that heat consistently elevates HR beyond the effects observed when menthol is swilled in Cold conditions.

[La] values demonstrated *trivial* reductions in response to menthol mouth swilling in Cold conditions, at all sub-maximal speeds, however [La] values were higher upon time trial completion in Cold+M condition ($0.7 \pm 0.9 \text{ mmol.L}^{-1}$; ES: 0.31 ± 0.43).

Differences between Hot and Hot+M were non-uniform across sub-maximal speeds, but displayed a pronounced reduction post-time-trial when menthol was swilled in the heat ($-2.3 \pm 3.1 \text{ mmol.L}^{-1}$; ES: -1.08 ± 1.44). [La] values in Hot were elevated when compared to Cold at all speeds, despite no differences prior to test commencement, again this difference was greatest upon time trial completion ($2.6 \pm 3.4 \text{ mmol.L}^{-1}$; ES: 1.2 ± 1.57). When menthol mouth-swilling conditions are compared (Cold+M vs. Hot+M), all speeds display wider confidence intervals than their respective standardised mean differences but there is a tendency for [La] to be elevated. This heat induced increase in [La] is also evident in remaining comparisons, with the greatest magnitudes of difference seen when Cold and Hot+M conditions are compared (Table 7.2).

7.3.2 Subjective Measures

7.3.2.1 Differential Ratings of Perceived Exertion

In Cold conditions, menthol mouth swilling (Cold+M) tended to increase dRPE values, particularly in RPE_{lung} and RPE_{over} , but these effects had confidence intervals overlapping

zero. All dRPE values were elevated following completion of the time trial in Cold+M ($RPE_{over} 3.6 \pm 5.8$; $RPE_{legs} 4 \pm 5.2$; $RPE_{lung} 5.4 \pm 9.2$. All differences reported as arbitrary units).

Large (-1.99 ± 1.57) reductions in RPE_{over} upon time trial completion (-14 ± 11.1 arbitrary units) was seen when menthol was swilled in the heat (Hot+M). This effect was likely a manifestation of reductions in RPE_{legs} (-9.5 ± 11.4 arbitrary units) and RPE_{lung} (-4.5 ± 11.2 arbitrary units). These effects were not observed at lower speeds in the heat (Hot vs. Hot+M).

Heat (Hot) tends to elevate RPE_{over} in comparison to Cold conditions, but this is not supported by other dRPE values, except for RPE_{lung} which upon time trial completion is *moderately* elevated (ES: 0.69 ± 0.56) in Hot+M conditions. When menthol mouth swilling conditions are compared (Cold+M vs. Hot+M) there is no apparent trend in dRPE values at sub-maximal speeds, but dRPE values and effects were lower in Hot+M upon time trial completion, albeit with broad confidence intervals. No clear trends were observed for remaining comparisons.

7.3.2.2 Thermal Comfort, Sensation and Thirst

Raw differences of TC, TS and Thirst for comparisons within temperatures (Cold vs Cold+M and Hot vs Hot+M) and Cold vs. Hot conditions are presented in Figure 7.1.

TC may be improved in Cold+M relative to Cold, with menthol induced reductions in TS also seen at lower speeds, whereas thirst is lowered on average at higher running speeds (Figure 7.1). Counterintuitively, in Hot conditions menthol mouth swilling (Hot+M) may elevate TS and thirst, whilst also improving TC, although these effects are highly variable. Between temperatures (Cold vs. Hot) TS is elevated to a *Large* to *Very Large* extent, with greater effects observed at lower running speeds (Table 7.2). Despite the clear differences in TS, differences in TC and thirst are not as consistent between temperatures. When menthol containing conditions are compared (Cold +M vs. Hot+M), TS is elevated in Hot+M, the difference (2.8 ± 0.6 to 1 ± 0.5) and magnitude (*Very Large* to *Large*) of which also declines as exercise intensity increases. Differences in TC are unclear, with differences in Thirst between Cold+M and Hot+M also variable. Similar elevations in TS brought about by heat are seen in remaining comparisons, with or without menthol mouth swilling (Cold vs Hot+M and Cold+M vs Hot), with tendencies toward a decrease in TC and Thirst also noted.

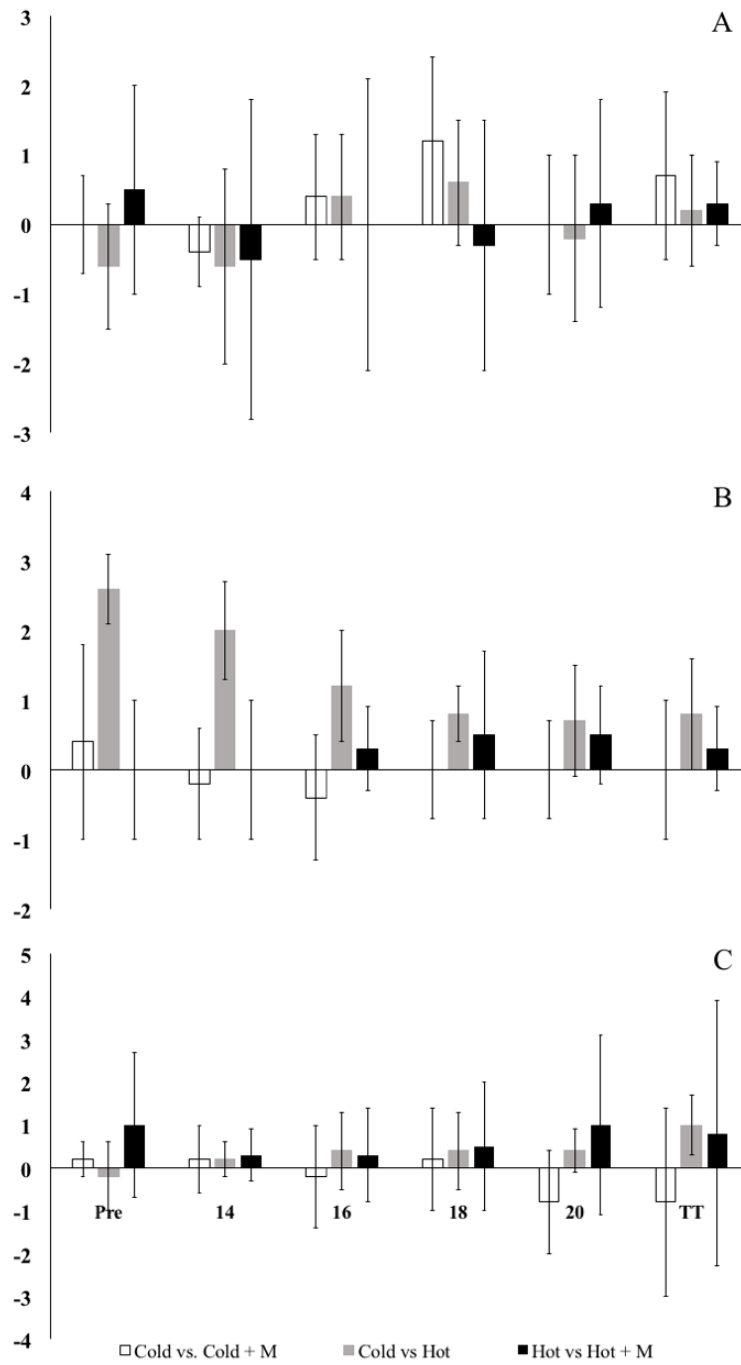
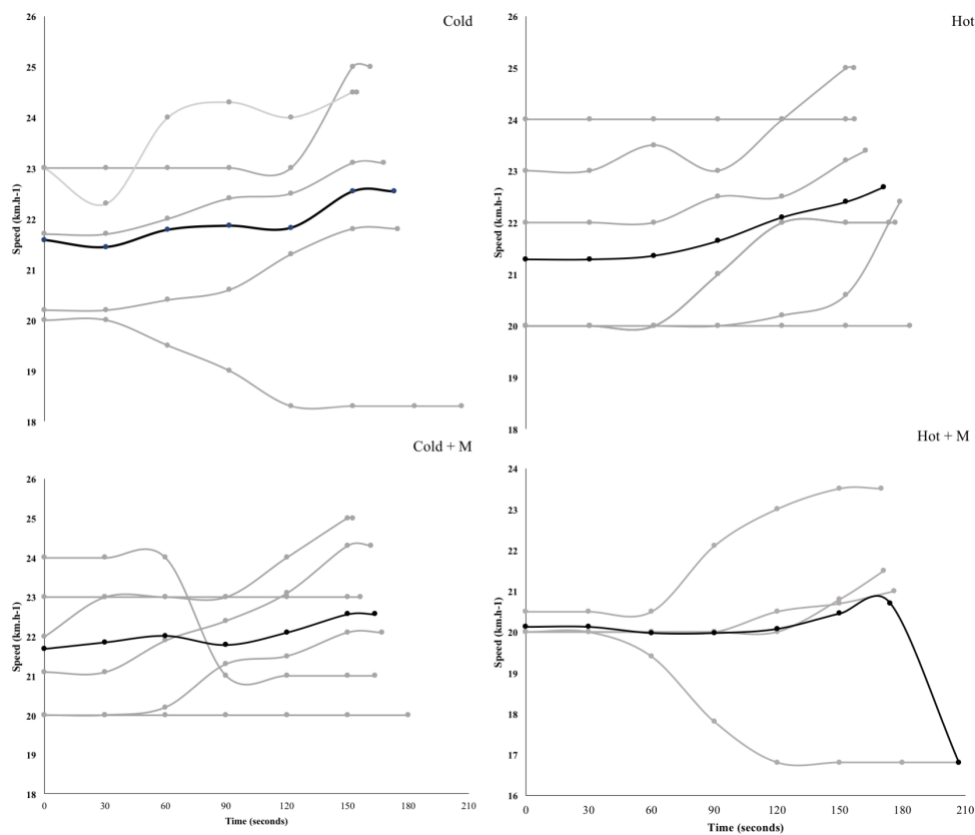


Figure 7-1 Raw differences (mean \pm standard deviations; arbitrary units) in Thermal Comfort (Panel A), Thermal Sensation (Panel B) and Thirst (Panel C) at baseline and throughout the testing protocol, within and between temperatures. Numeric values are xkm.h-1; TT: *Time Trial*

7.3.3 Time Trial Performance

Within cold conditions (Cold vs. Cold+M) differences in time trial performance were unclear (-0.28 ± 0.56). Increases in time trial performance of equal measure were seen when Hot+M and Hot, and Hot and Cold+M conditions were compared ($+4.1 \pm 7.2$ seconds; ES: 0.22 ± 0.39). Heat exerted a deleterious effect on time trial performance i.e. Hot and Cold (0.35 ± 0.22 ; *Small*) and Hot+M and Cold (0.35 ± 0.22 ; *Small*), with differences between menthol treatment conditions the most pronounced but showing the greatest variability: Hot+M and Cold+M (0.71 ± 0.61 ; *Moderate*). Individual and mean pacing profiles per condition (Figure x; panels A-D), and between condition mean pacing profiles (Figure 7.3; panel E) are depicted below. Data are also shown with the outlying athlete removed (Figure 7.3; panels A-D) and how this influenced mean responses (Figure 7.3; panel E).



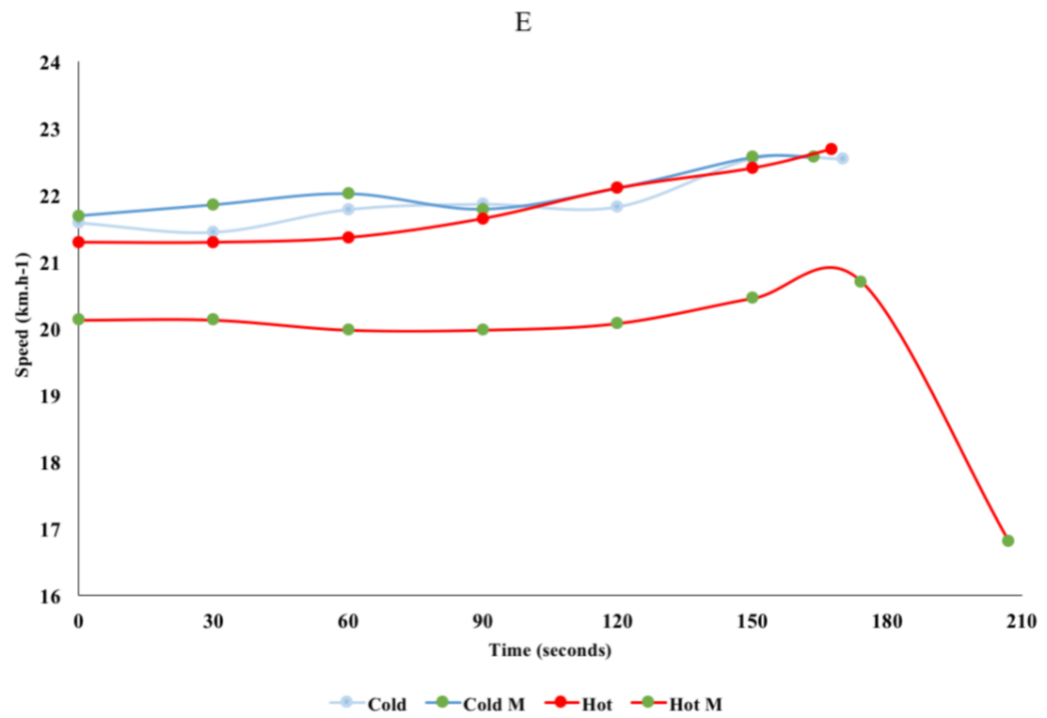
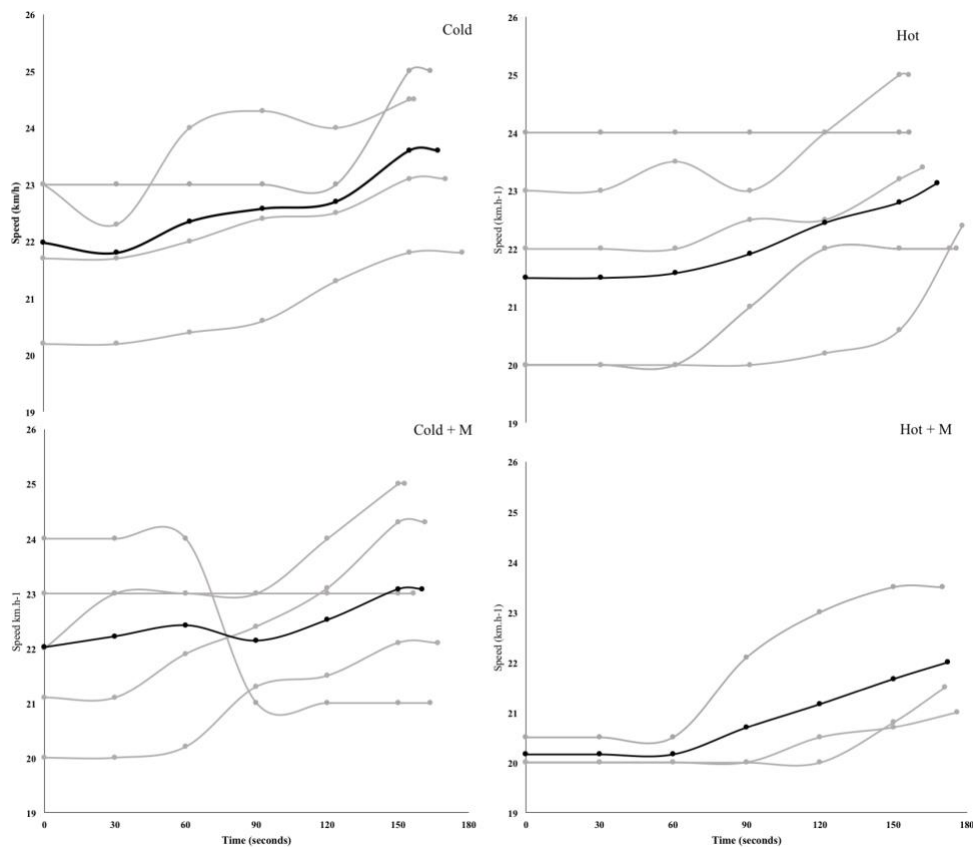


Figure 7-2 Individual and mean (Panel E) 1km time trial performances in Cold (Panel A) and Hot (Panel C) conditions, with (Panel B: Cold + M; Panel D: Hot + M) and without menthol mouth swilling. Standard deviations are not presented in Panel E due to the presentation of individual curves in panels A-D.



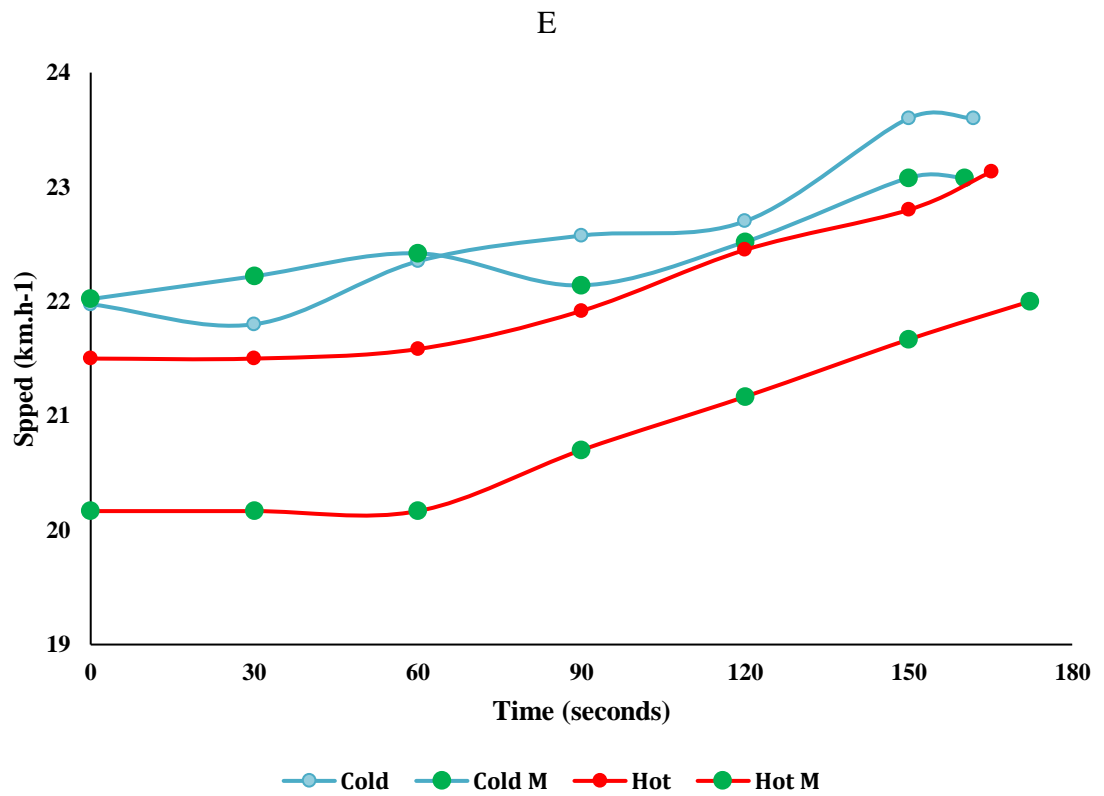


Figure 7-3 Individual and mean (Panel E) 1km time trial performances in Cold (Panel A) and Hot (Panel C) conditions, with (Panel B: Cold + M; Panel D: Hot + M) and without menthol mouth swilling, with the outlying athlete removed. Standard deviations are not presented in Panel E due to the presentation of individual curves in panels A-D.

Table 7-3 Effect Size and 90% Confidence Intervals for all outcome measures, with the exception of time trial performance, as compared between conditions and temperatures, plus remaining contrasts

Parameter	Cold vs. Cold+M	Cold vs. Hot	Hot vs. Hot+M	Cold+M vs. Hot+M	Cold+M vs. Hot	Cold vs. Hot+M
<i>14km.h⁻¹</i>						
$\dot{V}O_2$	0.25 ± 1.01	-0.04 ± 0.68	-0.02 ± 0.8	-0.11 ± 1.03	-0.13 ± 0.74	-0.04 ± 0.68
$\dot{V}E$	-0.23 ± 0.58	-0.93 ± 0.8*	0.24 ± 0.49	0.33 ± 0.55	0 ± 0.47	-0.09 ± 0.53
HR	0.34 ± 0.41	0.95 ± 0.65*	0.1 ± 0.61	0.27 ± 1.13	0.69 ± 0.66*	0.61 ± 0.29*
[La]	-0.30 ± 0.66	0.53 ± 1.02	-0.72 ± 2.02	0.35 ± 1.76	0.73 ± 0.47*	0.14 ± 1.08
T _{tymp}	0.30 ± 0.54	1.28 ± 0.17*	-0.15 ± 1.29	1.02 ± 1.18	0.98 ± 0.41*	1.17 ± 1.48
RPE _{over}	0.07 ± 0.3	0.04 ± 0.74	0.18 ± 1.41	-0.21 ± 1.17	-0.02 ± 0.76	-0.06 ± 1.13
RPE _{legs}	-0.08 ± 0.47	-0.20 ± 0.78	0.03 ± 1.59	-0.13 ± 1.57	0.26 ± 0.97	-0.13 ± 1.44
RPE _{lung}	0.19 ± 0.25	-0.32 ± 0.69	0.32 ± 1.59	-0.24 ± 1.10	-0.21 ± 0.58	0 ± 1.24
TC	-0.45 ± 0.59	0.38 ± 0.82	-0.57 ± 2.55	-0.49 ± 0.73	-0.76 ± 1.37	-0.81 ± 0.38
TS	-0.29 ± 1.17	2.92 ± 0.98*	0 ± 1.4	2.92 ± 0.79*	2.73 ± 1.16*	2.34 ± 0*
Thirst	0.36 ± 1.43	0.36 ± 0.76	0.45 ± 1.05	0 ± 1.13	0.28 ± 0.83	0.41 ± 0.56
<i>16km.h⁻¹</i>						
$\dot{V}O_2$	0.07 ± 0.93	0.17 ± 1.02	0.01 ± 0.87	-0.1 ± 0.65	-0.19 ± 0.21	-0.05 ± 0.79
$\dot{V}E$	-0.40 ± 0.34*	-0.43 ± 0.56	0.06 ± 0.16	0.35 ± 0.46	0.14 ± 0.75	-0.11 ± 0.10
HR	1.35 ± 1.95	1.65 ± 0.53*	0.63 ± 0.69	0.27 ± 1.13	0.73 ± 1.24	2.25 ± 1.60*
[La]	0.21 ± 0.63	0.50 ± 0.29*	0.23 ± 0.45	0.57 ± 0.86	0.26 ± 0.36	0.78 ± 0.17*
T _{tymp}	0.35 ± 0.60	1.59 ± 0.53*	-0.16 ± 0.56	1.33 ± 1.33	1.18 ± 0.65*	1.61 ± 1.06*
RPE _{over}	-0.32 ± 0.80	0.48 ± 0.99	-0.62 ± 2.07	-0.51 ± 0.83	0.28 ± 0.96	-0.67 ± 0.50*
RPE _{legs}	-0.37 ± 0.60	-0.39 ± 0.79	0 ± 1.12	-0.02 ± 0.74	0.28 ± 0.68	-0.26 ± 0.25*
RPE _{lung}	-0.15 ± 0.69	-0.32 ± 0.69	-0.04 ± 0.9	-0.4 ± 0.71	-0.07 ± 0.53	-0.34 ± 0.29*

TC	0.38 ± 0.50	0.38 ± 0.82	0 ± 2.05	0.18 ± 1.28	-0.60 ± 1.33	0.36 ± 1.1
TS	-0.72 ± 1.53	2.15 ± 1.43	0.45 ± 1.5	$4.02 \pm 1.05^*$	$2.68 \pm 1.54^*$	$2.68 \pm 1.22^*$
Thirst	-0.19 ± 1.19	0.38 ± 0.92	0.24 ± 1.08	0.34 ± 1.04	0.57 ± 0.83	$0.51 \pm 0.40^*$
<hr/> <i>18km.h-1</i>						
$\dot{V}O_2$	0.49 ± 1.16	-0.02 ± 0.93	0.19 ± 1.48	-0.35 ± 0.92	-0.46 ± 0.80	0.02 ± 0.79
$\dot{V}E$	-0.04 ± 0.88	-0.41 ± 0.55	0.15 ± 0.33	-0.25 ± 0.36	0.04 ± 0.27	0.33 ± 0.88
HR	1.35 ± 1.95	$0.67 \pm 0.53^*$	0.03 ± 0.69	0.2 ± 0.28	0.20 ± 0.28	0.67 ± 0.88
[La]	-0.09 ± 0.2	0.23 ± 0.14	0.14 ± 0.28	-0.02 ± 0.24	$0.32 \pm 0.23^*$	$0.41 \pm 0.35^*$
T _{tymp}	0.69 ± 1.31	$1.86 \pm 0.76^*$	0.08 ± 0.12	$1.49 \pm 1.35^*$	$1.16 \pm 0.80^*$	$2.18 \pm 0.85^*$
RPE _{over}	0.17 ± 0.84	0.70 ± 1.15	-0.62 ± 2.07	-0.1 ± 1.2	-0.09 ± 0.96	0.21 ± 0.24
RPE _{legs}	0.13 ± 1.2	0.21 ± 1.48	-0.49 ± 2.39	-0.33 ± 2.04	0.50 ± 0.89	0 ± 1.89
RPE _{lung}	0.33 ± 0.78	0.02 ± 0.40	0 ± 0.59	-0.46 ± 0.87	0.15 ± 0.48	0.08 ± 0.35
TC	1.15 ± 1.19	0.57 ± 0.82	-0.24 ± 1.32	-0.48 ± 1.55	-0.85 ± 0.98	0.16 ± 0.72
TS	0 ± 0.98	$1.17 \pm 0.62^*$	0.73 ± 1.72	1.77 ± 1.79	1.18 ± 0.87	$1.77 \pm 1.39^*$
Thirst	0.19 ± 1.19	0.38 ± 0.82	0.48 ± 1.45	0.28 ± 1.38	0.37 ± 0.86	$0.56 \pm 0.54^*$
<hr/> <i>20km.h-1</i>						
$\dot{V}O_2$	0.35 ± 0.83	-0.33 ± 0.71	0.19 ± 1.34	-0.51 ± 1.17	-0.73 ± 0.84	-0.38 ± 0.87
$\dot{V}E$	-0.09 ± 0.31	$-0.32 \pm 0.27^*$	0.22 ± 0.54	0.18 ± 0.42	0.04 ± 0.32	-0.10 ± 0.43
HR	0.16 ± 0.66	$0.49 \pm 0.49^*$	-0.17 ± 0.61	0.03 ± 1.04	0.43 ± 0.35	0.14 ± 1.04
[La]	-0.09 ± 0.26	0.20 ± 0.32	-0.13 ± 0.19	0.28 ± 0.40	$0.28 \pm 0.27^*$	0.08 ± 0.48
T _{tymp}	0.59 ± 0.61	$2.40 \pm 0.71^*$	-0.11 ± 0.63	$1.13 \pm 1.07^*$	$1.77 \pm 0.67^*$	2.40 ± 0.77
RPE _{over}	0.21 ± 0.37	0.21 ± 0.98	-0.06 ± 1.66	0.04 ± 0.33	0.06 ± 0.46	0.31 ± 0.42
RPE _{legs}	0 ± 0.52	0.12 ± 0.73	-0.15 ± 0.34	0.07 ± 0.17	0.34 ± 0.52	0.07 ± 0.76
RPE _{lung}	0.3 ± 0.52	0.05 ± 0.52	0.23 ± 0.37	-0.03 ± 0.59	-0.09 ± 0.47	0.31 ± 0.50
TC	0 ± 0.85	-0.18 ± 0.11	0.22 ± 1.32	0 ± 0.59	-0.41 ± 0.61	-0.15 ± 0.36

TS	0 ± 1.21	1.25 ± 1.43	0.89 ± 1.22	1.61 ± 1.91	1.18 ± 0.97	$1.61 \pm 1.45^*$
Thirst	-0.34 ± 0.53	0.17 ± 0.22	0.43 ± 0.92	-0.38 ± 1.03	$0.91 \pm 0.75^*$	0.75 ± 1.40

ES \pm 90 C.I. that do not overlap zero are denoted with an asterisk (*). Descriptors for magnitude of effects can be found in section 7.2.4 as per (Hopkins *et al.*, 2009)

Table 7-4 Effect Size and 90% Confidence Intervals for all outcome measures, with the exception of time trial performance, as compared between conditions and temperatures, plus remaining contrasts during 1km time trial stage

Parameter	Cold vs. Cold+M	Cold vs. Hot	Hot vs. Hot+M	Cold+M vs. Hot+M	Cold+M vs. Hot	Cold vs. Hot+M
$\dot{V}O_2$	0.14 ± 0.90	-10.9 ± 7.7	-0.47 ± 1.70	-0.26 ± 0.59	-0.50 ± 0.51	-0.08 ± 0.46
$\dot{V}E$	-0.21 ± 0.32	$-0.44 \pm 0.30^*$	0.11 ± 1.09	$-0.60 \pm 0.59^*$	-0.14 ± 0.48	$-0.82 \pm 0.34^*$
HR	$0.54 \pm 0.50^*$	0.17 ± 0.69	-0.52 ± 1.13	-0.62 ± 1.32	-0.26 ± 0.58	-0.38 ± 1.23
[La]	0.31 ± 0.43	1.2 ± 1.57	-1.08 ± 1.44	0.03 ± 0.77	0.66 ± 1.06	0.28 ± 0.99
T _{t ymp}	$1.01 \pm 0.58^*$	2.02 ± 0.87	$-0.56 \pm 0.38^*$	0.75 ± 1.57	$1.05 \pm 0.95^*$	$1.53 \pm 1.24^*$
RPE _{over}	0.51 ± 0.83	0.02 ± 0.87	$-1.99 \pm 1.57^*$	-0.89 ± 1.72	0.28 ± 0.73	-0.07 ± 1.62
RPE _{legs}	0.41 ± 0.53	0.61 ± 0.63	-0.97 ± 1.16	-0.79 ± 1.14	0.17 ± 0.24	-0.20 ± 0.81
RPE _{lung}	0.55 ± 0.93	$0.69 \pm 0.56^*$	-0.45 ± 1.13	-0.45 ± 1.13	0.17 ± 0.24	0.40 ± 0.76
TC	0.79 ± 1.41	0.23 ± 0.90	0.28 ± 0.67	0.20 ± 0.46	-0.46 ± 0.66	0.39 ± 0.53
TS	0 ± 1.39	$1.17 \pm 1.17^*$	0.37 ± 0.86	$1.46 \pm 0.76^*$	1.46 ± 0.76	$1.83 \pm 0.86^*$
Thirst	-0.42 ± 1.15	$0.53 \pm 0.36^*$	0.4 ± 1.63	-0.38 ± 1.03	1.11 ± 0.98	0.83 ± 1.15

ES \pm 90 C.I. that do not overlap zero are denoted with an asterisk (*). Descriptors for magnitude of effects can be found in section 7.2.4 as per (Hopkins *et al.*, 2009)

7.4 Discussion

The aim of this study was to assess the effects of menthol mouth swilling upon performance and physiological and perceptual characteristics at running speeds and temperatures pertinent to British athletes. We did this by adapting Saunders' RE protocol to incorporate speeds that were representative of competitive and training velocities, specifically adding a 20km.h⁻¹ stage, and a 1km time trial (Saunders, Pyne, Telford and Hawley, 2004b). The inclusion of these speeds allowed a more rigorous assessment and quantification of the oxygen cost of running in trained athletes and increased the potential for positive findings to be applied ecologically. The inclusion of a time trial provided a testing element that was reflective of competitive running environments by incorporating a variable pace component to the testing procedure. This is best exemplified in Figures 7.2 and 7.3, which outline the mean and individual pacing strategies adopted by each competitor, with most athletes displaying an 'end spurt' and or inverse pacing profile (Tucker, Lambert and Noakes, 2006; Van Biesen *et al.*, 2016). Testing of similar durations to the time trial have previously been shown to be reliable in runners (Pettitt, Jamnick and Clark, 2012; Gama *et al.*, 2017; McGawley, 2017; Gama *et al.*, 2018), and may be used to predict performance through estimation of critical power (Vanhatalo, A.M. Jones and Burnley, 2011; Burnley and A.M. Jones, 2018; Gama *et al.*, 2018). Time trials also typically show greater reliability than time to exhaustion tests (Laursen *et al.*, 2007; Stevens and Dascombe, 2015) due to lack of confounding influences. However, time trials also require a commitment to producing a maximal effort, which may present a mismatch between performance capacity and the anticipatory performance template (Tucker, 2009; Foster *et al.*, 2009).

The time trial data from this study are counterintuitive, and counter the evidence accrued to date, which has shown menthol to improve running performance (Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016), albeit over 5km as opposed to 1km. In Hot+M this may be a statistical artefact, due to low participant numbers of lesser ability (5km PB mean) completing this trial. All participants exhibit a similar performance curve with a substantial increase in pace in the latter half of the time trial once the outlier is removed; this is not sufficient to offset the lower mean speed in the first 60 seconds in comparison to Hot conditions, and again runs counter to previous findings. This conservative start may be driven by an interaction between the observed increase in $\dot{V}E$ and RPE_{lung} values at 20km.h⁻¹ in Hot+M conditions. Whilst an increase in $\dot{V}E$ has previously been reported as concomitant to the beneficial effects of menthol mouth swilling (Mündel and D. A. Jones, 2009; Stevens and Best, 2017), in better trained athletes an increase in $\dot{V}E$ brought about

by menthol use may drive an increase in RPE_{lung} due to a heightened awareness of respiratory frequency, synonymous with exercise induced fatigue, irrespective of environmental conditions. This may also aid in explaining the perceived increase in thirst at higher speeds when Hot and Hot+M conditions are compared (Figure 7.2, Panel C), although the wide standard deviations around these values are acknowledged.

In Cold+M athletes were 6.5 seconds faster on average over 1km than in the Cold condition (Figure 7.2, Panel E); this reduced to 1.59 seconds when the outlier was removed (Figure 7.3, Panel E), and so likely falls within the coefficient of variation for the performance. The pacing strategy adopted by athletes in the cold is seemingly more aggressive, yet even paced, displaying a faster starting velocity and less of an end spurt than in hot conditions. This difference in strategies is addressed by Tucker and in part by Van Biesen (Tucker, Lambert and Noakes, 2006; Van Biesen *et al.*, 2016) as the difference between middle and long distance pacing strategies: in Cold and Cold+M conditions our athletes display pacing characteristic of 800 and 1500m runners, yet as temperature increases (Hot) and menthol possibly increases awareness of this (Hot+M) the participants' pacing profile reverts to a long distance style i.e. an even early pace, with a large end spurt (Tucker, Lambert and Noakes, 2006). This behaviour suggests that pacing strategy is a product of multi-sensory inputs, as per an interoceptive model of fatigue (Stevens and Best, 2017; McMorris, Barwood and Corbett, 2018), and may either possess a default template that one reverts to under challenging circumstances, or if these inputs are ignored be at risk of premature exhaustion as shown above (Figures 7.2 and 7.3). Pacing strategies vary dependent upon event duration (Abbiss and Laursen, 2008) and may also be indicative of athlete ability (Sandals *et al.*, 2006; Abbiss and Laursen, 2008; Hettinga *et al.*, 2010). Indeed, pacing is a learned behaviour which improves with repeat exposure to the same task (Foster *et al.*, 2009). This effect has been reported to be most notable in the early stages of exercise (Foster *et al.*, 2009), independent of exercise modality.

The variety of pacing strategies during the time trials suggest an inhibition of a central governor (Tucker *et al.*, 2006) or regulatory feed-forward mechanism (Jay and Kenny, 2009), possibly due to lack of feedback provided to the athlete during the trial in comparison to more ecologically valid settings. The athlete must instead interpret the signals sent from multiple inputs ($dRPE$, HR, $[La]$, $\dot{V}E$ and perceived running speed) in lieu of sensory feedback such as visual cues, audible 'splits', or the presence of competition (Corbett *et al.*, 2017), limiting knowledge or prediction of exercise end-point. The influence of heat on such a regulatory model (Jay and Kenny, 2009), and performance,

is affected by training status (Mora-Rodriguez, 2012; McLellan *et al.*, 2012; Lisman *et al.*, 2014), degree of heat acclimation (Junge *et al.*, 2016; Stevens *et al.*, 2017) and exercise modality (Mora-Rodriguez, Ortega and Hamouti, 2011; Junge *et al.*, 2016), and so is best assessed across multiple exposures to the same temperature(s) whilst controlling for factors such as wind-speed, humidity and clothing.

The elevation in HR under mentholated conditions observed within this study is a novel finding. Contrary to previous literature (Mündel and D. A. Jones, 2009; Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016; Flood, Waldron and Jeffries, 2017), elevated HR was observed in both Cold+M and Hot+M conditions. These differences are possibly harmful from baseline in both conditions, but diminish in Hot+M at higher speeds. Although not an explanation for the elevated HR at lower speeds, there is a concomitant elevation in $\dot{V}E$ and diminution in HR, T_{tymp} , [La], and dRPE values at 20km.h⁻¹ and upon 1km time trial completion in Hot+M. The addition of menthol may have driven the increase in $\dot{V}E$, as per other works (Mündel and D. A. Jones, 2009; Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016), and the athlete(s) adjusted their pace in line with this signal, explaining the reduction in other physiological variables. Specifically, the increased awareness (manifested as an elevated RPE_{lung}) brought about by an increased $\dot{V}E$ in combination with menthol induced sensitisation of the oral cavity, led to a slower starting velocity (Figure 7.2 and 7.3, Panels D and E) during the 1km time trial and this is responsible for a lag in other physiological values, in comparison to other conditions.

In Cold+M it is plausible that this possibly harmful difference in HR from baseline and throughout the testing protocol may have inadvertently facilitated time trial performance, but hindered RE, as shown by an increase in $\dot{V}O_2$, elevated T_{tymp} and further confirmed subjectively by increased dRPE values. This notion is supported by the pacing profile adopted by most athletes in this condition, apart from one athlete who ran aggressively early in the trial, before fading. Whilst not a positive performance outcome for that athlete, this suggests that in this instance menthol mouth-swilling may possess qualitative factors or influences not examined in the present study.

The elevated HR can be likened to the anticipatory rise (Aubert, Seps and Beckers, 2003), which is then further compounded by the novel stimulus of a menthol mouth-swill. Menthol has the potential, through stimulation of TRPA1 receptors, to activate the sympathetic nervous system. When coupled with a psycho-physiological anticipatory effect due to the application a novel stimulus and resultant increase in $\dot{V}E$, an elevated HR is much more readily explained. Indeed, the application of menthol has been repeatedly described as capable of inducing arousal (Eccles, 2000a; Eccles *et al.*, 2013), the

magnitude of which is likely to correlate with the thickness of the outermost layer of the skin i.e. the stratum corneum (H. R. Watson *et al.*, 1978; Patel, Ishiuchi and Yosipovitch, 2007; Stevens and Best, 2017). The increase in HR cannot be ignored and warrants further investigation with repeat exposures in Cold+M conditions, to assess whether HR habituation occurs across subsequent exposures, although thermally-mediated perceptual and physiological characteristics may also affect this response.

Within Cold temperatures, menthol mouth swilling evoked increases in TC of 0.4 ± 0.9 , 1.2 ± 1.2 , and 0.7 ± 1.2 arbitrary units at 16km.h⁻¹, 18km.h⁻¹ and upon 1km time trial completion respectively. In national and elite distance runners, the lower speeds have been shown to be satisfactorily reliable in RE and other physiological values (Saunders, Pyne, Telford and Hawley, 2004b), increasing confidence that the change in thermal comfort is driven by the use of menthol. The improvement in TC in response to menthol mouth swilling may be considered pleasurable by some athletes; intra-oral temperature stimuli, such as menthol, have the ability to confer a hedonic effect (Eccles *et al.*, 2013) by stimulating a network of taste and reward-responsive regions of the brain (Rolls, 2010). Indeed TC may be subjectively defined as ‘that condition of mind which expresses satisfaction with the thermal environment.’ (Epstein and Moran, 2006); operationally defined TC is the interpretation of thermal inputs (Schulze *et al.*, 2015) that may drive behavioural thermoregulation (Frank *et al.*, 1999). The latter of the two definitions accounts for physiological factors that may influence TC and may be a product of fitness as reflected in the present study in Hot conditions. Differences in TC are less uniform when Hot conditions are compared. This may be attributed to varying degrees of heat acclimation within the group, or differing sensitivity to menthol. This sensitivity may be induced by the experiment (acute) and therefore would parallel an increase in T_{tymp}, or the result of inheritance of a TRP gene variant (chronic (Morgan *et al.*, 2014; Morgan, Sadofsky and Morice, 2015)).

Mechanistically, menthol elicits a cooling sensation through stimulation of TRM8 receptors and the trigeminal nerve in the oral cavity (Eccles, 2000). The perceived magnitude of this response may be heightened if local temperature (T_{tymp}) is also elevated in response to exercise and swilling, as we have observed. Menthol has been shown to increase the perception of cold in other beverages for five minutes when swilled at a 0.02% concentration (Green, 1985), so any water drunk *ad libitum* during the trial(s) may also have been perceived as more refreshing, and thirst quenching (Eccles, 2000; Eccles *et al.*, 2013) despite the water volume(s) consumed most likely being insufficient to offset exercise induced changes in plasma osmolality (Eccles, 2000), partially explaining the

limited change in thirst values observed throughout the trial(s). Thirst values may also be blunted by an increase in salivary flow rate brought about by mouth-swilling (Dawes, 1987; Eccles, 2000) which may have provided a hygro-sensory stimulus. This effect is diminished in the heat, due to evaporative and respiratory water losses likely exceeding the counter-sensory stimulus provided by menthol. This may have been further exacerbated by the low humidity (10%) coupled with Hot temperature (28°C) and the potential for the alcohol within the mouth swill to evaporate and potentially contribute to 'dry-mouth' (Dawes, 1987), so thirst was or remained elevated relative to Hot conditions without menthol. Thirst needn't be present to induce a feeling that is perceived as pleasant (Eccles, 2000), as evidenced by changes in TC and TS.

Thermal Sensation clearly differed between temperatures, although this difference diminished as exercise intensity increased, most likely due to the greater amount of heat being produced because of the metabolic and mechanical work being completed to attain higher running speeds (Maughan, 1984; Junge *et al.*, 2016). In Cold conditions, when exercising, menthol appeared to improve thermal sensation by lowering athletes' perception up to 18km.h⁻¹, beyond which responses became unclear. However, in Hot conditions, menthol showed little influence on TS at lower speeds and increased TS at higher speeds. The ability of menthol to enhance warmth has been noted previously by Green (Green, 1985), when the oral cavity was cooler than the menthol solution that was swilled. Menthol was stored in the same chamber as the participant in this investigation to be representative of an *aid station* in a race. This move toward ecological validity may have hindered the efficacy of the solution.

The varied responses, as evidenced by large standard deviations across measures of thermal perception, suggest either an individual tolerance to menthol, or that trained athletes are less susceptible to the perceptual and thermal challenges of exercise than lesser trained populations (Cheung and McLellan, 1998; Mora-Rodriguez, 2012; McLellan *et al.*, 2012; Lisman *et al.*, 2014). This is not to be confused with athletes not presenting as responders to menthol, but that contrary to previous research the response is bidirectional. Differences within variables were observed at a range of speeds with little uniformity between or within temperatures. Sixteen kilometres per hour (16km.h⁻¹) has previously been suggested to be of importance as it has been historically used to assess the RE of a wide-range of athletes (J. Daniels and N. Daniels, 1992; Saunders, Pyne, Telford and Hawley, 2004b; A.M. Jones, 2006) against supporting reference values (Barnes and Kilding, 2015), and is a commonly encountered speed in training (A. M. Jones, 2006). Our data support recommendations that 16km.h⁻¹ presents an interesting and potentially

important speed at which to assess RE and associated measures, but the variety of differences and unclear responses observed suggest the need for testing based upon individualised aerobic parameters e.g. $\dot{V}O_{2max}$, $v\dot{V}O_{2max}$ and lactate threshold (LT) (Joyner and Coyle, 2008). These unclear responses are likely further compounded by the low sample size of the present investigation.

Individualisation can be achieved by adopting either a ‘clamped’ or graded approach. In a clamped approach RPE or the dRPE input considered to be limiting is prescribed hence ‘clamped’, and physiological and subjective responses beyond this measure are assessed throughout the exercise bout. This model has been used in environmental physiology research previously, with (Flood, Waldron and Jeffries, 2017) and without (Tucker *et al.*, 2006) menthol mouth swilling. A graded approach may more closely resemble this investigation methodologically. However, exercise intensities are prescribed based upon individual work rates such as percentage $\dot{V}O_{2max}$ or $v\dot{V}O_{2max}$, or haematological thresholds such as 2mmol.L⁻¹ and 4mmol.L⁻¹ [La] (Hall *et al.*, 2016), although these have been shown to be unreliable (Aunola and Rusko, 1984; Hall *et al.*, 2016) relative to $\dot{V}O_{2max}$ and associated percentages (Mann, Lamberts and Lambert, 2013). There is some confusion as to nomenclature when discussing physiological thresholds generally (Keir *et al.*, 2015; Hall *et al.*, 2016), so if training is to be individualised and fitness tracked longitudinally, it must be done so holistically and described using multiple metrics, at pertinent intensities, as per case studies of elite distance runners (A. M. Jones, 1998; 2006; Lucia *et al.*, 2008). Alternatively, if laboratory based testing is not available to the athlete or coach, testing may involve assessing performance and dRPE responses during a standardised training session.

Variability within participant physiology, and manifestation thereof is further evidenced by the range within participant 5km personal best (range: 2 min 8 sec), despite our participants being considered well-trained or elite by academic standards (De Pauw and Roelands, 2013; Barnes and Kilding, 2015) and faster than those previously studied by Stevens (Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016). Whilst literature may categorise these athletes based upon physiological values, these values manifest themselves as stark differences in real world running performance, further emphasising the need for individualisation. This is perhaps best expressed by an equation for distance running performance (as per a physiological model):

$$\dot{V}O_{2max} \times \text{lactate threshold} \times \text{running economy}$$

(Joyner, 1991; Joyner and Coyle, 2008)

Given the contrasting environmental conditions investigated, and the susceptibility for temperature to affect distance running performance (Maughan, 1984; Maughan, Watson and Shirreffs, 2007; Maughan, 2010), the ventilatory and lactate responses observed within this study may be in part explained by the effects of temperature and heat storage upon the physiological variables described above.

Temperature is often cited as a determining factor in exercise performance in the heat, with a critical value of a core temperature (T_{core}) of 40°C typically posited (Ely *et al.*, 2009). Multiple case reports (Maughan, 1984) and laboratory investigations (González Alonso *et al.*, 1999; Ely *et al.*, 2009; Cuddy, Hailes and Ruby, 2014; Corbett *et al.*, 2017) counter this assertion, suggesting instead that the rate of heat accumulation sustained by an individual, and their perception thereof, may drive reductions in exercise performance. Elevation of core temperature is considered a function of work, but is susceptible to influence from exercise nature (Mora-Rodriguez, Del Coso and Estevez, 2008) and modality (Mora-Rodriguez, Ortega and Hamouti, 2011). Specifically, intermittent exercise leads to a greater rate of heat accumulation than continuous exercise, when matched for exercise duration. Intermittent exercise also elevates $\dot{V}O_2$ to a greater extent than continuous exercise, concomitantly impairing sweat rate hereby impairing heat dissipation. Ecologically this is evidenced by the preference for even or negative pacing strategies by athletes, which likely confer energetic and thermoregulatory advantages. (Kraning and Gonzalez, 1991; Morris *et al.*, 1998; 2000)

Heat accumulation, heat storage and the temperature gradient between an athlete's core and periphery (a driver of sweat rates) can all be mitigated by the ingestion of cooling strategies such as ice slurries (M.L. Ross, Garvican and Jeacocke, 2011; Stevens *et al.*, 2013; Levels *et al.*, 2013; Stevens, Thoseby, *et al.*, 2016; Maunder, Laursen and Kilding, 2016) and cold liquid (Riera *et al.*, 2014; Tran Trong *et al.*, 2015; Maunder, Laursen and Kilding, 2016; Jay and Morris, 2018). Yet menthol has been documented to improve running performance in this study and others (Tran Trong *et al.*, 2015; Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016), independent of these changes, suggesting that cooling of the oral cavity, and therefore stimulation of the trigeminal nerve and TRPM8 receptors, by subjective or physiological means, may confer a benefit to performance.

The considerations raised above indicate that individualised approaches to athlete assessment in thermally challenging conditions warrant further investigation. Clamping of dRPE presents an easy and practical method of individualising athlete assessment, suggesting a continuous exercise modality is preferred. A comparison between established

physiological cooling strategies and menthol would further advance understanding as to the potential importance of the oral cavity in ergogenic cooling strategies adopted by athletes.

CHAPTER 8 : SWILLING OF PHYSIOLOGICAL AND PERCEPTUAL COOLING AGENTS DURING A SIMULATED RUNNING TRAINING SESSION IN THE HEAT

Menthol has previously been administered during time to exhaustion protocols, short time trials or to extend time to exhaustion following a period of fixed work. Such protocols are generally considered representative of competition, but may not be indicative of preparing for competition, thus assessing menthol's physiological and perceptual effects during a simulated training session may be of benefit to athletes e.g. undergoing acclimation or warm weather training preparations. Four male athletes completed a graded exercise test, to establish the velocity corresponding to 2mmol [La] and the accompanying RPE_{legs} value, which served as a dRPE 'clamp' that athletes had to sustain throughout three, 30min simulated training sessions. Trial order was assigned randomly, with athletes asked to swill either ice, menthol, or no swill (control) at 5 min intervals throughout the simulated session, conducted in hot conditions (35°C, 10% humidity). Athletes were free to change running speed, but RPE_{legs} was to remain clamped for the session duration. Measures of $\dot{V}O_2$, $\dot{V}E$, HR, [La], T_{tymp} TC, TS, Th, were also assessed at 5 min intervals throughout the session. Large to very large reductions in $\dot{V}O_2$ occurred in the latter half of the session following menthol mouth swilling, independent of changes in $\dot{V}E$, T_{tymp} and dRPE values. Perceptually, ice swilling induced greater changes in TC and thirst than menthol compared to not swilling; menthol exposure also induced more moderate alterations in these variables at similar time points. Other single time point differences or trends did occur but were predominantly considered unclear. Athletes' running speed remained consistent throughout all trials suggesting appropriate clamping of RPE_{legs} and minimal variation. To conclude, menthol mouth swilling may present a feasible and practical alternative to ice slurry swilling during exercise of 30min, in hot environmental conditions in trained runners, although a larger sample size is required to confirm these results.

8.1 Introduction

Athletes employ a range of cooling methodologies, at varying time points throughout an exercise bout to combat perceived and physiological thermal strain imparted by exercising in hot conditions (Bongers *et al.*, 2014; Hopman, Bongers and Eijssvogels, 2017; Best, Payton, *et al.*, 2018). This strain may be compensable or non-compensable (Givoni and

Goldman, 1972; Cheung, McLellan and Tenaglia, 2000). Compensable heat strain refers to the body being able to maintain a steady thermal state, whereas, non-compensable heat strain suggests that one or more of conductive, convective, evaporative and radiative cooling mechanisms may be impaired (Givoni and Goldman, 1972; Maughan, 1984; Cheung, McLellan and Tenaglia, 2000). Both types of strain may lead to compromised exercise performance (Maughan, 1984; González Alonso *et al.*, 1999; Cheung, McLellan and Tenaglia, 2000), and may also detract from associated tasks such as decision making (Schmit, Duffield and Hausswirth, 2015; Schmit *et al.*, 2017) and wider cognitive function (Corbett *et al.*, 2017; Watkins *et al.*, 2018), that may have a bearing on competitive outcome. The nature of the heat stress to be experienced by an athlete should inform the cooling strategy administered during the exercise bout, with athlete preference and tolerance of such strategies also pertinent factors.

The term used throughout this thesis to describe one's combined perceptual and physiological state is that of interoception, where one posits 'How do I feel now?' (Craig, 2002); this question is pivotal in exercise, as it challenges an athlete to interpret *exteroceptive* somatosensory signals, *interoceptive* drives and emotional/motivational qualities (A.D. Craig, 2003), which ultimately manifest in an athlete's performance. Interestingly, an athlete's perception of their physiological condition can be deceived (Castle *et al.*, 2012; H. S. Jones *et al.*, 2013; D. N. Borg *et al.*, 2018). It is established that with the appropriate administration of perceptual (Stevens and Best, 2017; Best, Payton, *et al.*, 2018; Jeffries and Waldron, 2018) and / or physiological (Quod, Martin and Laursen, 2006; M.L. Ross *et al.*, 2013; Bongers *et al.*, 2014; Stevens, Taylor and Dascombe, 2016; Hopman, Bongers and Eijssvogels, 2017; Best, Payton, *et al.*, 2018) cooling interventions an athlete's performance can be augmented, yet the possible influence of deception in environmentally challenging conditions (Castle *et al.*, 2012; H.S. Jones *et al.*, 2013; D. N. Borg *et al.*, 2018) suggests that tending to an athlete's interoception may elicit greater ergogenic effects, with respect to heat tolerance, than simply addressing physiological limitations in isolation. Indeed, whilst an athlete's interoceptive state may dictate or limit their performance outcome, the system(s) is perhaps fallible.

Given menthol's ability to alter thirst as outlined by Eccles (Eccles, 2000) and evidenced in chapter six, this suggests menthol can impart effects that tend to an athlete's interoception when exercising in a hot environment, evoking a sensation of "I feel cooler". In contrast, a physiological cooling agent such as ice, typically induces a lower T_{core} and so would elicit a response of "I am cooler" by an athlete. Such a distinction may be important for athletes preparing to compete in the heat to be able to make, given the

potential risk of heat injury and associated illness, if training for prolonged times in thermally challenging conditions.

Much of the research regarding cooling interventions, irrespective of cooling modality, has tended to employ an exhaustive protocol, whether that be time to exhaustion at a fixed intensity (Mitchell, McFarlin and Dugas, 2003; Mündel *et al.*, 2006; Mündel and D. A. Jones, 2009) or rating of perceived exertion (Schlader, Stannard and Mündel, 2011; Flood, Waldron and Jeffries, 2017; Bright *et al.*, 2019), or a time trial of a predetermined duration (Quod *et al.*, 2008; Duffield *et al.*, 2010; Byrne *et al.*, 2011; Gonzales *et al.*, 2014), or distance (Stanley, Leveritt and Peake, 2010; M.L. Ross, Garvican and Jeacocke, 2011; Muñoz *et al.*, 2012; Riera *et al.*, 2014; Stevens, Thoseby, *et al.*, 2016). Very few authors have investigated designs that replicate typical training sessions undertaken by endurance athletes in the heat (Kenny *et al.*, 2009; Tran Trong *et al.*, 2015), and those that have (Maxwell, Aitchison and Nimmo, 1996; Kenny *et al.*, 2009; Tran Trong *et al.*, 2015) employed submaximal workloads that may not mirror the training demands of athletes preparing to compete in the heat, or undertaking warm weather training trips, implying either that the investigations lack ecological validity or that the athletes involved in most investigations are not in fact trained when considered against more robust criteria (De Pauw and Roelands, 2013). It is also acknowledged that there may be ethical and experimental considerations that have also influenced environmental physiology investigations to date (Cheung, McLellan and Tenaglia, 2000).

Identification of the preferred and / or most effective cooling strategy in an ecologically valid setting (session duration, environment and intensity) in trained athletes would be of benefit to athletes undergoing acclimation or warm weather training preparations. Practically, whether this strategy is perceptual (menthol) or physiological (ice) in nature, may have important logistical ramifications for an athlete and associated support staff due to the resources required to ensure a strategy is appropriately administered, at an appropriate temperature. Hence, the aim of this investigation is to assess the effects of menthol mouth swilling in comparison to ice mouth swilling, during a 30-minute training session in trained distance runners.

8.2 Materials and Methods

This study employed a post-only crossover design, in which participants served as their own controls. Experimental effects were derived from between condition comparisons and individual responses to each condition over time. Ethical approval for this investigation

was granted by the Teesside University School of Social Sciences, Business and Law ethics board.

Prior to study commencement, participants completed a graded exercise test to assess $\dot{V}O_{2\max}$, the velocity at which $\geq 2\text{mmol}$ blood lactate ([La]) occurred and corresponding dRPE values, as per the CR100 scale (E. Borg and G. Borg, 2002). These data were used to individualise exercise intensity during simulated training sessions, as we adopted a ‘clamped’ RPE model (Tucker *et al.*, 2006; Flood, Waldron and Jeffries, 2017), corresponding to the RPE_{legs} obtained when $\geq 2\text{mmol}$ [La] was obtained, as this value represents a minor but sustainable increase in [La] above baseline levels and corresponds to the aerobic threshold (Mann, Lamberts and Lambert, 2013). This session also served to familiarise participants with the experimental warm-up procedure and testing environment.

Nutritional intake was recorded via a 24-hour food recall preceding the first experimental session, with participants encouraged to consume a typical diet throughout the testing period. The 24-hour recall served as a template that participants aimed to replicate throughout the testing period, with a view to increasing experimental and ecological validity. Experimental sessions (one visit per condition: Control, Ice, Menthol) comprised three laboratory visits, with trial order assigned via a Latin square design, as per a customised spreadsheet (Pezzullo, 1999). All experimental sessions took place in an environmental chamber, with participants wearing a harness in case of involuntary collapse when exercising. Temperature was set at 35°C for all trials; humidity was fixed at 10% and wind speed at 0 m.s^{-1} to mitigate cooling effects driven by environmental factors beyond temperature and to maximise individuals’ rates of heat storage. Water was available *ad-libitum* at room temperature during exercise.

8.2.1 Participants

Four male athletes undertook this investigation; participant information is presented below (Table 8.1). Testing sessions were incorporated into the participants’ training schedule by their coach and would replace a weekly ‘tempo’ session. Training volume was requested to be maintained throughout the testing battery, so results would be indicative of each athlete’s typical abilities, and not the product of an increase or reduction in training volume. Athletes wore their preferred training clothing e.g. shorts and singlet and racing flats to increase ecological validity and athlete comfort.

Table 8-1 Participant anthropometric, physiological and performance characteristics

Participant #	Age (years)	Height (cm)	Weight (kg)	$\dot{V}O_{2\max}$ (ml.kg ⁻¹ .min ⁻¹)	5km PB (mm:ss)	5km Speed (km.h ⁻¹)
1	18.9	177.0	64.0	65.5	16:28	18.22
2	17.1	170.0	58.0	65.5	15:46	19.03
3	18.1	175.0	66.4	67.6	15:43	19.09
4	20.8	175.0	56.0	67.8	15:37	19.21
Mean \pm SD	18.7 \pm 1.38	174.3 \pm 2.59	61.1 \pm 4.25	66.61 \pm 1.29	15:53 \pm 00:20	18.89 \pm 0.39

8.2.2 Simulated training session

The simulated training session was broken down into five-minute intervals for analysis purpose, but comprised 30 min continuous running in total. Outcome measures were recorded at the intervals depicted in the diagram below (Figure 8.1). Each training session was preceded by a 10 min warm-up at 10km.h⁻¹ on the same make and model treadmill (h/p/cosmos Pulsar; h/p/cosmos Sports & Medical GMBH; Nussdorf-Traunstein, Germany) that the training session was completed upon. Athletes cooled down on the same treadmill, for the same duration at a self-selected intensity. Physiological cooling was provided by swilling an ice-slurry mixture for 10-seconds prior to expectoration. Ice slurry was made from 150g ice and 200ml water, blended in a vortex mixer (Thermomix ®; Vorwerk & Co. KG, Wuppertal, Germany). Menthol was diluted as previously described (Best, Spears, *et al.*, 2018), and provided at a 0.1% concentration to be swilled for 10-seconds. Swilling took place whilst running to simulate a continuous training session, or aid stations.

8.2.3 Outcome Measures

8.2.3.1 Physiological Measures

$\dot{V}O_2$ (ml.min⁻¹ and ml.kg⁻¹.min⁻¹) and VE (L.min⁻¹) were assessed using breath by breath analysis (Piston HD6000, nSpire, nSpire Health Inc, Hertford, UK), for the final two minutes of each five-minute interval. Breath by breath $\dot{V}O_2$ was averaged over for each stage. From this data was filtered using conditional formatting to obtain 30 seconds of data that was \pm 50ml from the mean. This method was chosen as steady state oxygen consumption has previously been defined as an increase of <100ml O₂ over the final two minutes of the stage (Fletcher, Esau and MacIntosh, 2009). Samples to be analysed for [La] were obtained from the non-dominant ring-finger using a lancet and collected in a capillary tube for automated analysis by a YSI 2700 Select analyser (YSI (UK) Ltd., Hampshire, United Kingdom) via a 25 μ L sample. Heart rate values were recorded 30

seconds prior to stage completion using telemetry (Polar RS400; Polar, Helsinki, Finland). Temperature was recorded prior to the test session, and upon completion of five-minute segment. Temperature was assessed using a tympanic thermometer ($\pm 0.1^{\circ}\text{C}$; Braun Thermoscan 5; Braun, Braun GmbH, Kronberg, Germany) and disposable caps, with measures taken from the left ear. Temperature was assessed following administration of menthol and ice, so any potential increase in temperature caused by swelling or local temperature reduction would be recorded.

8.2.3.2 Subjective Measures

Subjective measures were assessed using validated rating scales, with accompanying descriptors. Thirst was assessed via Engell's scale (Appendix 3; (Engell *et al.*, 1987), ranging from 'Not at all thirsty' to 'Extremely thirsty'. Zhang *et al.*'s scales of TC and TS were used to assess these qualities (Appendix 2 (Zhang *et al.*, 2004). Both scales range from -4 to +4, with polar descriptors of Very Uncomfortable: Very Comfortable, and Very Cold: Very Hot, respectively. As a point of difference, the TC scale contains values of -0 and +0 to numerically describe just uncomfortable and just comfortable, respectively (Zhang *et al.*, 2004). Borg's CR100 scale (E. Borg and G. Borg, 2002) with idiomatic English verbal descriptors (Appendix 1) was used to assess dRPE. This differential approach clamped RPE at the legs (RPE_{legs}), and assessed RPE for the lungs ($\text{RPE}_{\text{lungs}}$) and overall (RPE_{over}).

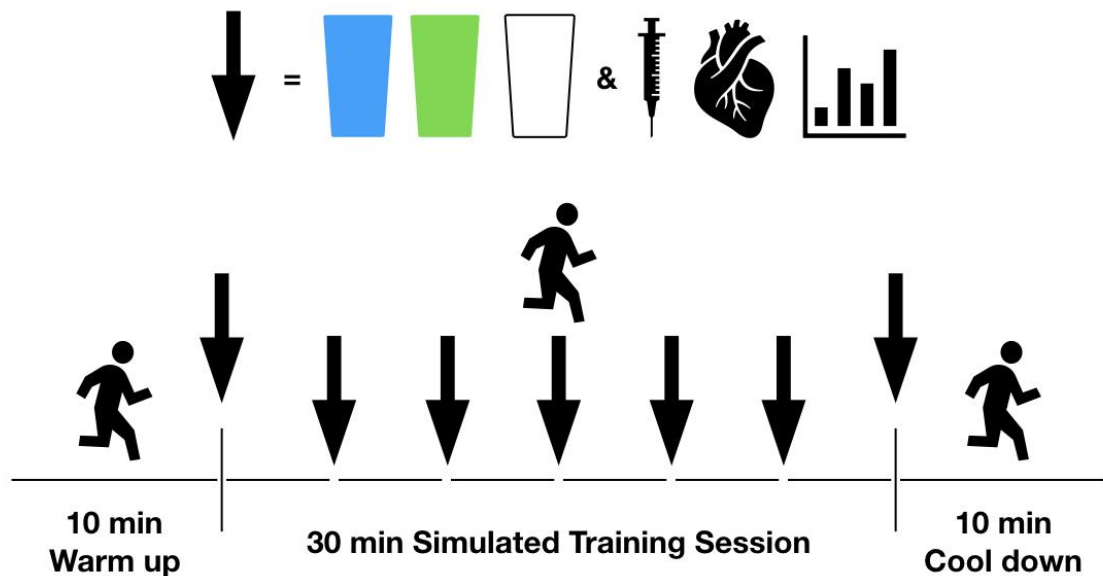


Figure 8-1 Testing Protocol for each trial. Downward arrows indicate the application of randomised swill (Blue and Green glasses represent ice and menthol respectively. The clear glass represents the control condition), and assessment of outcome measures ([La], HR and dRPE values, as per symbols left to right)).

8.2.4 Statistical analyses

Data were analysed using standardised mean differences, via a customised spreadsheet (Hopkins, 2006). Magnitudes of effects were based upon standardised thresholds for *Small* (0.2), *Moderate* (0.6), *Large* (1.2) and *Very Large* (2.0) changes of standardised mean differences (Hopkins *et al.*, 2009), irrespective of outcome measure. Raw data are presented as mean \pm SD. Standardised mean differences are presented as effect sizes (ES) \pm 90% confidence intervals (C.I.). Per condition each athletes' $\% \dot{V}O_{2\max}$ elicited by their self-selected running speed (km.h⁻¹) was plotted over the session duration at five-minute intervals and presented with an accompanying R^2 value (0-1). This allowed for a more meaningful expression of exercise intensity between conditions, accounting for internal and external load, despite a clamped RPE_{legs}. Further, a customised spreadsheet for the analysis of individuals (Hopkins, 2017) was used to derive an individual slope per athlete, per condition for TC, TS and thirst. This approach allowed an understanding of the likelihood of each athlete experiencing a substantial change in TC, TS, and thirst at five-minute intervals throughout the exercise bout, whilst accounting for minimal important differences and typical error within each variable (Hopkins, 2017). If a change was deemed to be *likely* substantial, it represented a 75% chance of change (Hopkins, 2017) in either a

positive or negative direction. Minimal important differences for TC, TS and thirst were considered to be 0.5 units.

8.3 Results

Running speed throughout each trial remained relatively stable on average, between time points and between conditions. This is supported by standard deviations greater than the change in mean(s), and confidence intervals that overlap zero, relative to the effect statistic (Tables 8.2 - 8.4). Relationships between % $\dot{V}O_{2max}$ and running speed are presented in Figure 8.2, with accompanying R^2 values also stated, where possible; in the incidence of no change in running speed throughout the exercise bout the relationship is solely represented pictorially.

8.3.1 Physiological Measures

Both menthol and ice slurry lowered $\dot{V}O_2$ throughout the exercise bout, with menthol demonstrating *large – very large* reductions of 4 – 4.3 ml.kg⁻¹.min⁻¹ in the latter half of the bout; ice slurry also lowered $\dot{V}O_2$, however the standardised mean difference only exceeded the standard deviation at trial completion (-3.1 ± 2.7 ml.kg⁻¹.min⁻¹; *Large*). Ventilation also responded to perceptual and physiological cooling but showed divergent responses to cooling stimuli with ice lowering $\dot{V}E$ throughout exercise duration, but failing to produce a meaningful effect, and menthol increasing $\dot{V}E$ by a *small* magnitude relative to ice slurry swilling, in the latter third of the training session.

Beyond respiratory measures, athletes who swilled ice slurry presented with lower HR in comparison to menthol at baseline (-14.0 ± 13.6 bpm; *Small*) but these effects dissipated throughout the tempo run. Blood lactate [La] showed a similarly *small* reduction in the ice slurry condition compared to menthol at baseline, with lower mean [La] values persisting between conditions but showing increased variability (as expressed via a greater standard deviation, and widening confidence intervals) as exercise duration increased, suggesting the attenuation or dissipation of these baseline differences in most athletes. No notable differences in T_{tymp} were found between cooling or control conditions at any time point.

8.3.2 Subjective Measures

Rating of perceived exertion measures were not different between conditions, suggesting that clamping of RPE_{legs} had a similar effect upon other differential RPE measures (RPE_{over} ; RPE_{lungs}).

Thermal Comfort responded most to ice slurry swilling when compared to the control session, demonstrating an improved thermal comfort from half-way through the exercise bout; these effects were *small – large* in nature, with a change of 0.8 – 1.5 raw units, representing one or more verbal descriptors. Menthol also showed a similar trend toward improving TC, however the effect statistic (0.55; *small*) only exceeded the confidence interval (± 0.43) upon session completion in comparison to the control session, but reduced variability was apparent from half-way through the tempo run (narrowing of standard deviations), highlighting the effects of menthol mouth swilling became more uniform over time. Despite contrasting magnitudes of effect, when compared directly ice slurry and menthol mouth swilling only differed notably at baseline (0.48 ± 0.47 ; *small*). With respect to TS, both menthol and ice slurry swilling lowered TS relative to control throughout the exercise bout, but these effects were considered *trivial* due to the range of responses observed. Similarly, when menthol and ice slurry ingestion were contrasted, ice slurry tended to lower TS, but considerable variability was observed. *Large – Very Large* reductions in thirst were observed at 5 and 10 min intervals following ice slurry application, however the uniformity and direction of these results altered over the course of the exercise bout. Menthol also lowered thirst by a *moderate* degree at 5 min in comparison to control (0.8 ± 0.6 AU) and tended to report higher values than ice slurry swilling when the two strategies are contrasted (Table 8.4). Individual trend lines for each variable are presented in Figures 8.3 - 8.5; changes that are substantially different (positive or negative) to the previous observation are marked with a §.

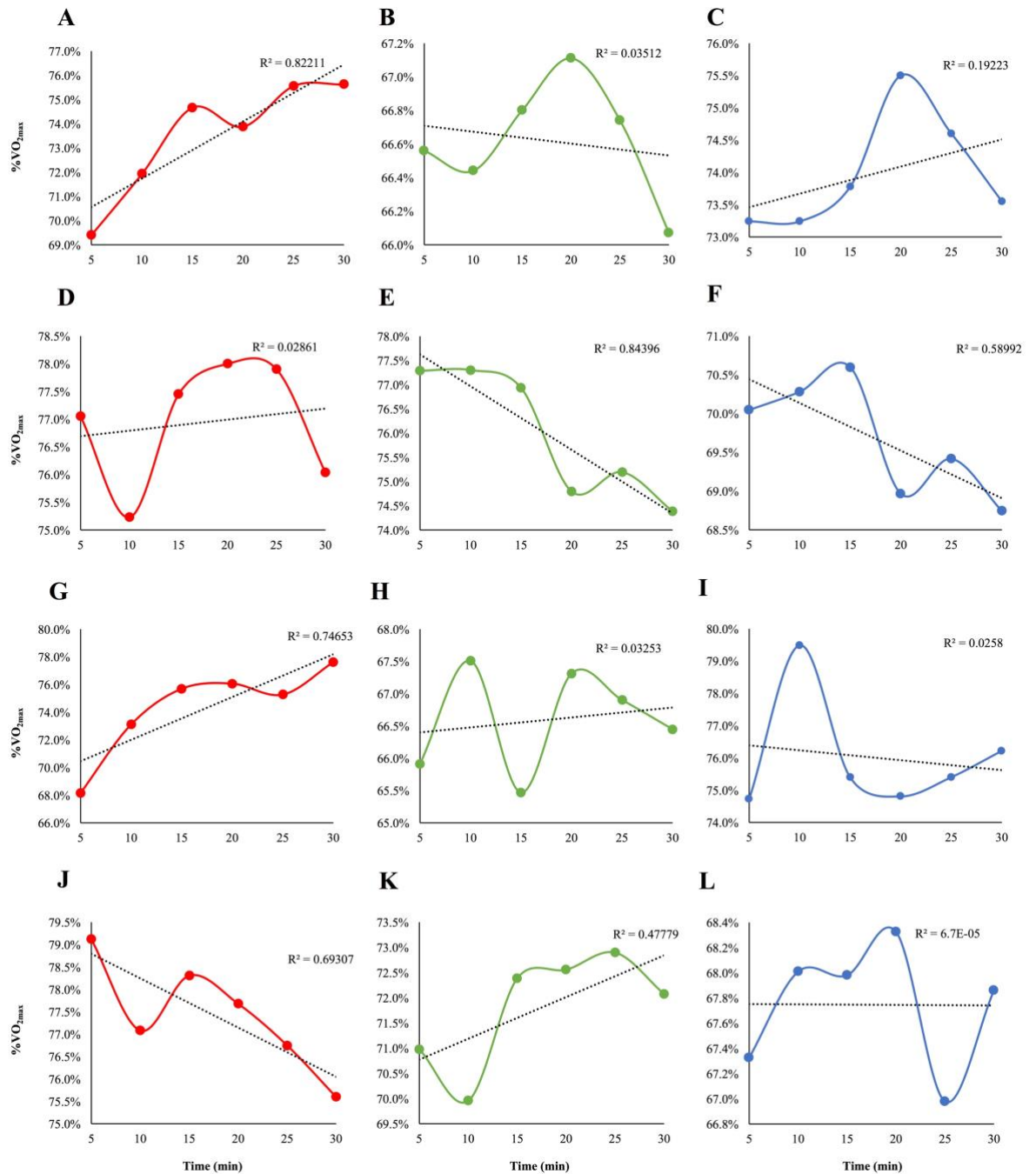


Figure 8-2 Oxygen uptake ($\dot{V}O_2$) as a percentage of $\dot{V}O_{2max}$ per each five-minute interval, over the 30-minute training session. Each horizontal series represents a different athlete, with each colour/ column representing a different condition (Left to right: Control, Menthol, Ice). Linear trend lines and R^2 values are shown to highlight individual variability, within and between conditions and as such the effect of each condition upon $\dot{V}O_2$ over time.

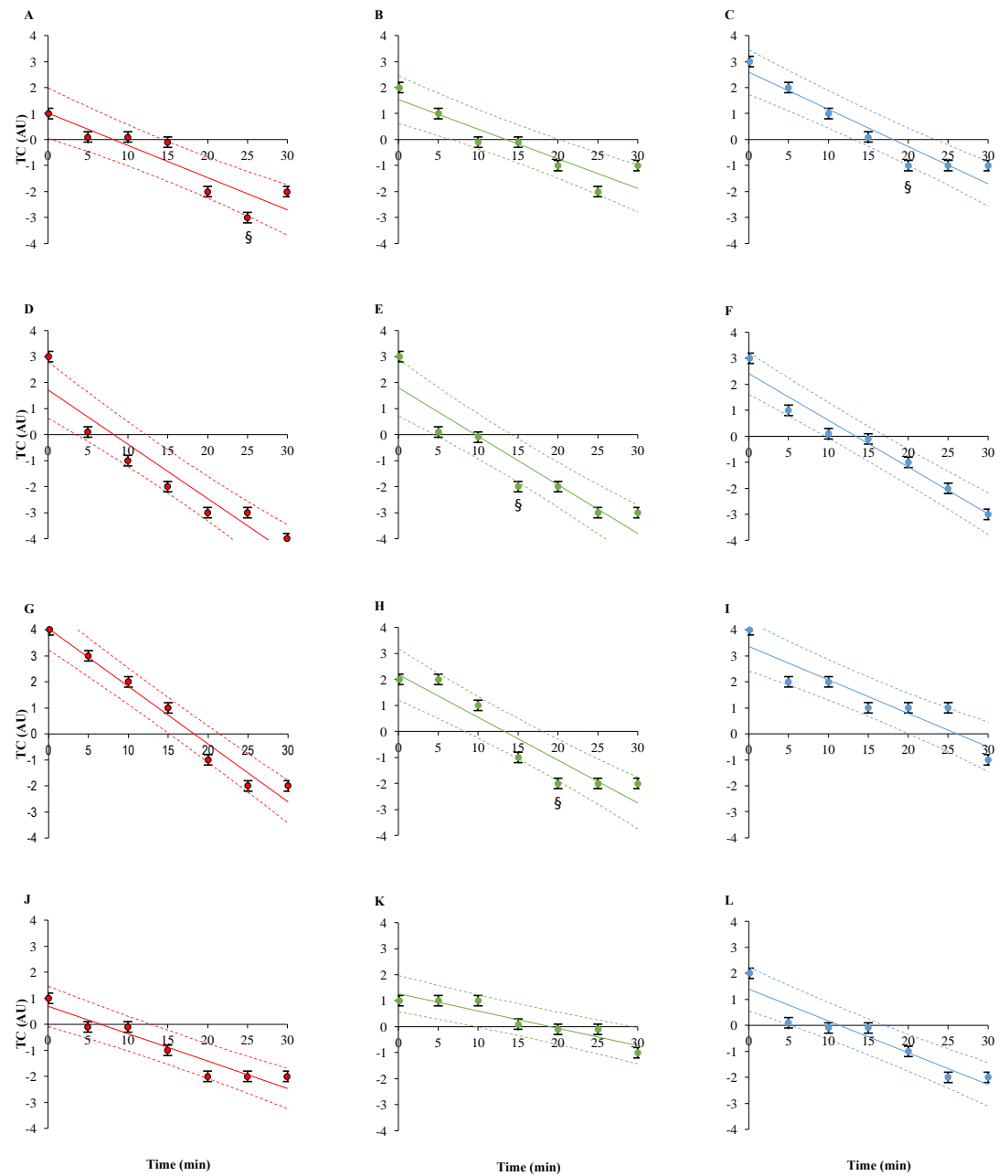


Figure 8-3 Individual trends in thermal comfort (AU) between conditions. Each horizontal series represents a different athlete, with each colour/ column representing a different condition (Left to right: Control, Menthol, Ice). The solid lines represent the trend for all data points, per athlete, per condition. Values that fall outside of the dashed lines represent a change that is deemed to be >75% likely substantial and are denoted by the following symbol §

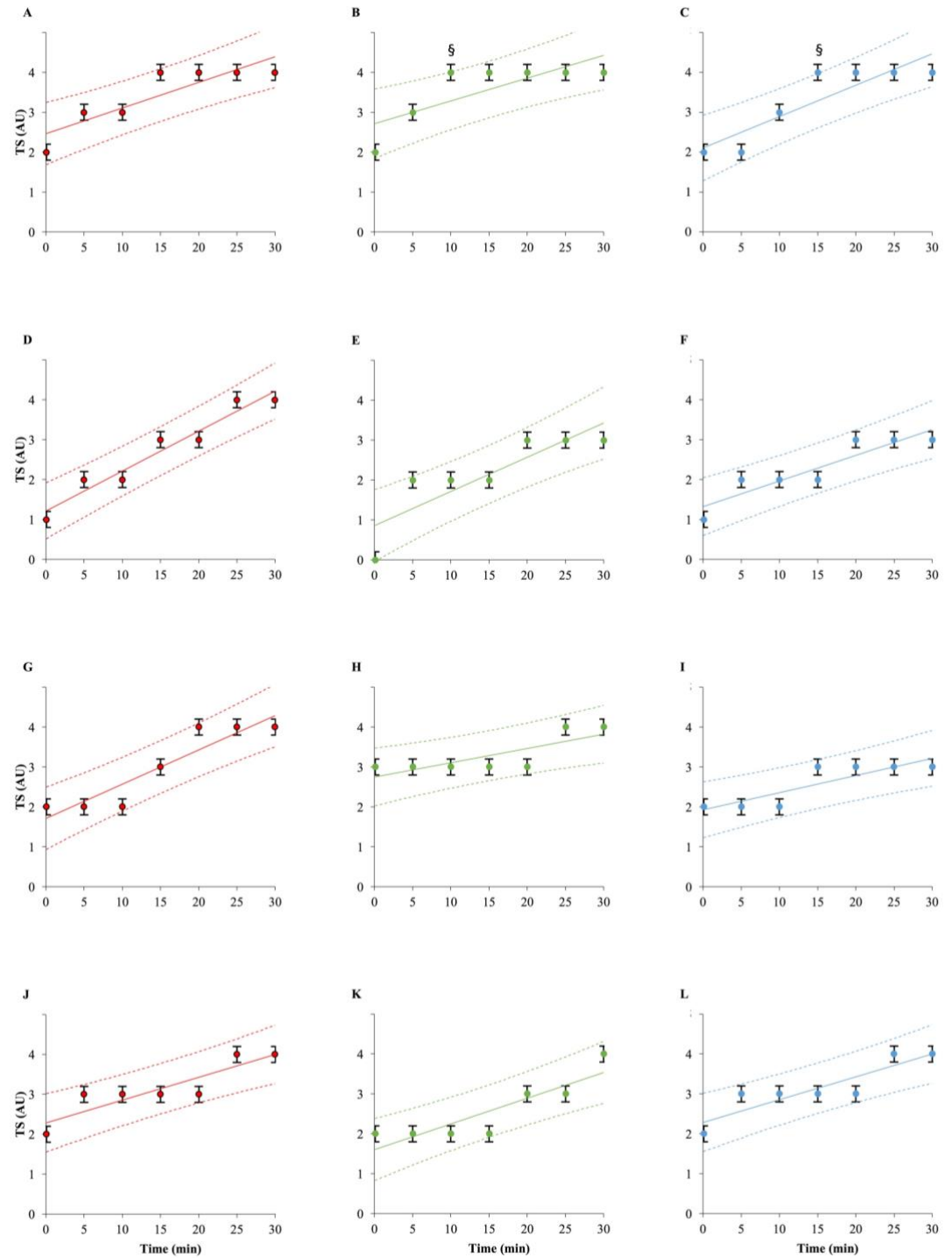


Figure 8-4 Individual trends in thermal sensation (AU) between conditions. Each horizontal series represents a different athlete, with each colour/ column representing a different condition (Left to right: Control, Menthol, Ice). The solid lines represent the trend for all data points, per athlete, per condition. Values that fall outside of the dashed lines represent a change that is deemed to be >75% likely substantial and are denoted by the following symbol §

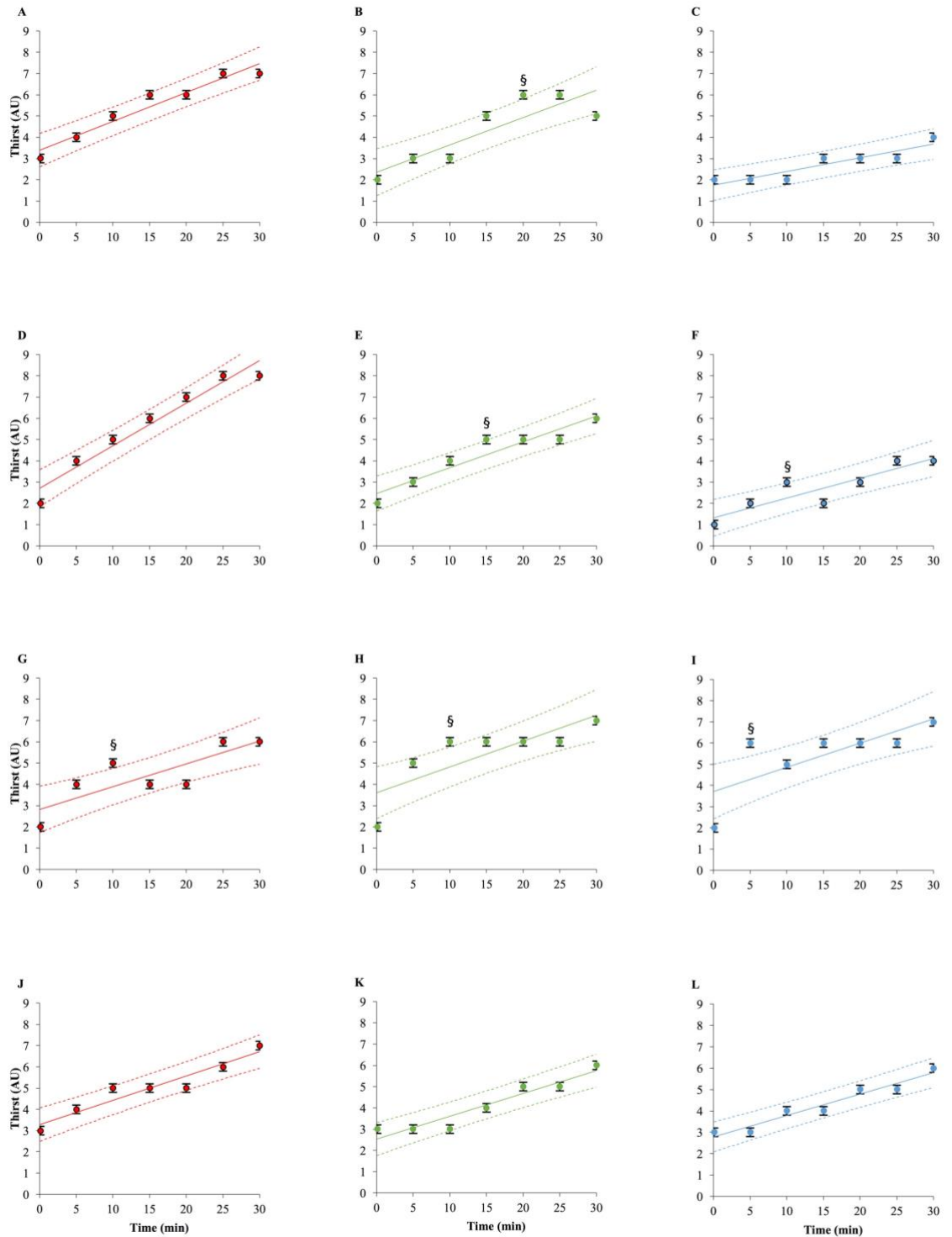


Figure.8-5 Individual trends in thirst (AU) between conditions. Each horizontal series represents a different athlete, with each colour/ column representing a different condition (Left to right: Control, Menthol, Ice). The solid lines represent the trend for all data points, per athlete, per condition. Values that fall outside of the dashed lines represent a change that is deemed to be >75% likely substantial and are denoted by the following symbol §

Table 8-2 Effects of menthol mouth swilling on physiological and perceptual variables at each time point throughout the testing bout. Variables with confidence limits that do not cross zero are in bold. Magnitude of the effect is denoted by the following symbols *: Small; # Moderate; †: Large; ‡: Very Large.

Variable	Comparison	Pre	5 min	10 min	15 min	20 min	25 min	30 min
$\dot{V}O_2$ (ml.kg ⁻¹ .min ⁻¹)	Raw difference	-	-2.2 ± 2.8	-2.7 ± 3.3	-4.1 ± 3.3	-4.0 ± 1.8	-4.0 ± 2.4	-4.3 ± 3.6
	ES ± 90% C.I.	-	-0.37 ± 0.48	-0.86 ± 1.04	-1.52 ± 1.21†	-1.31 ± 0.61†	-1.73 ± 1.04†	-2.37 ± 1.98‡
$\dot{V}E$ (L.min ⁻¹)	Raw difference	-	1.4 ± 5.0	-1.5 ± 5.0	-1.8 ± 8.0	1.0 ± 2.2	1.2 ± 4.3	-1.4 ± 8.3
	ES ± 90% C.I.	-	0.35 ± 1.23	-0.1 ± 0.34	-0.08 ± 0.36	0.06 ± 0.13	0.05 ± 0.19	-0.06 ± 0.34
HR (bpm)	Raw difference	1.7 ± 25.6	-2.0 ± 6.7	1.0 ± 3.5	4.8 ± 4.7	3.5 ± 4.8	1.3 ± 6	5.5 ± 4.0
	ES ± 90% C.I.	0.09 ± 1.32	-0.17 ± 0.57	0.08 ± 0.27	0.42 ± 0.42*	0.28 ± 0.37	0.1 ± 0.49	0.51 ± 0.37#
[La] (mmol.L ⁻¹)	Raw difference	1.1 ± 1.2	0.4 ± 1.5	0.9 ± 1.3	0.9 ± 1.9	1.6 ± 2.0	1.5 ± 1.5	1.1 ± 1.7
	ES ± 90% C.I.	0.87 ± 0.96	0.24 ± 0.99	0.72 ± 0.98	0.54 ± 1.15	0.82 ± 1.04	5.07 ± 5.2	1.60 ± 2.41
T_{tym} (°c)	Raw difference	0.0 ± 0.3	0.1 ± 0.2	0.0 ± 0.1	0.0 ± 0.5	0.0 ± 0.4	0.0 ± 0.4	0.2 ± 0.5
	ES ± 90% C.I.	0.07 ± 0.83	0.26 ± 0.50	0.07 ± 0.43	0.0 ± 1.51	0.73 ± 5.32	0.0 ± 0.87	0.43 ± 1.12
RPE _{over} AU	Raw difference	-	-0.5 ± 12.8	-0.3 ± 11.8	-0.8 ± 9.8	-1.3 ± 7.3	-0.3 ± 8.3	-0.3 ± 2.2
	ES ± 90% C.I.	-	-0.04 ± 0.93	-0.03 ± 1.37	-0.11 ± 1.48	-0.19 ± 1.12	-0.03 ± 0.97	-0.04 ± 0.38
RPE _{lungs} AU	Raw difference	-	-2.5 ± 12.2	-2.0 ± 11.5	-2.0 ± 10.0	1.3 ± 9.5	-1.8 ± 7.3	0.8 ± 3.5
	ES ± 90% C.I.	-	-0.24 ± 1.19	-0.40 ± 1.23	-0.28 ± 1.39	0.16 ± 1.20	-0.44 ± 1.85	0.19 ± 0.89
Thirst AU	Raw difference	-0.3 ± 0.6	-0.8 ± 0.6	-1.0 ± 1.7	-0.3 ± 1.8	0.0 ± 1.9	-1.3 ± 1.5	-1.0 ± 1.17
	ES ± 90% C.I.	-0.31 ± 0.74	-1.09 ± 0.86#	-1.00 ± 1.22	-0.19 ± 1.34	0.00 ± 1.08	-0.95 ± 1.12	-0.89 ± 1.48
TC AU	Raw difference	-0.3 ± 1.5	0.3 ± 1.2	0.0 ± 1.4	-0.1 ± 1.7	0.6 ± 1.3	0.6 ± 0.9	0.8 ± 0.6
	ES ± 90% C.I.	-0.12 ± 0.72	0.12 ± 0.60	0.00 ± 0.79	-0.07 ± 0.98	0.56 ± 1.16	0.79 ± 1.11	0.55 ± 0.43*
TS AU	Raw difference	0.0 ± 1.0	0.0 ± 1.0	0.3 ± 1.1	-0.5 ± 0.7	-0.3 ± 0.6	-0.5 ± 0.7	-0.3 ± 0.6
	ES ± 90% C.I.	0.00 ± 1.40	0.00 ± 1.21	0.31 ± 1.42	-0.73 ± 0.99	-0.31 ± 0.74	-1.22 ± 1.24	-0.71 ± 1.19
Speed (km.h ⁻¹)	Raw difference	-	0.0 ± 0.0	-0.2 ± 0.4	-0.2 ± 0.5	-0.2 ± 0.5	-0.2 ± 0.5	0.0 ± 0.4
	ES ± 90% C.I.	-	0.00 ± 0.00	-0.19 ± 0.32	-0.19 ± 0.40	-0.17 ± 0.36	-0.15 ± 0.33	0.03 ± 0.30

Table 8-3 Effects of ice swilling on physiological and perceptual variables at each time point throughout the testing bout. Variables with confidence limits that do not cross zero are in bold. Magnitude of the effect is denoted by the following symbols *: Small; # Moderate; †: Large; ‡: Very Large.

Variable	Comparison	Pre	5 min	10 min	15 min	20 min	25 min	30 min
$\dot{V}O_2$ (ml.kg ⁻¹ .min ⁻¹)	Raw difference	-	-1.5 ± 6.9	-1.1 ± 5.4	-3.1 ± 3.9	-3.1 ± 4.4	-3.2 ± 4.1	-3.1 ± 2.7
	ES ± 90% C.I.	-	-0.25 ± 1.18	-0.35 ± 1.72	-1.15 ± 1.43	-1.01 ± 1.45	-1.41 ± 1.77	-1.72 ± 1.48†
$\dot{V}E$ (L.min ⁻¹)	Raw difference	-	0.4 ± 8.0	-2.1 ± 9.7	-4.2 ± 10.3	-6.7 ± 4.7	-8.2 ± 11.2	-7.5 ± 11.4
	ES ± 90% C.I.	-	0.10 ± 1.94	-0.14 ± 0.65	-0.19 ± 0.46	-4.00 ± 0.27‡	-0.37 ± 0.50	-0.30 ± 0.47
HR (bpm)	Raw difference	-7.7 ± 30.4	-0.8 ± 11.3	2.3 ± 5.5	3.8 ± 6.3	3.3 ± 8.2	1.0 ± 9.1	4.3 ± 8.0
	ES ± 90% C.I.	-0.4 ± 1.57	-0.06 ± 0.96	0.18 ± 0.43	0.33 ± 0.56	0.26 ± 0.64	0.08 ± 0.74	0.39 ± 0.74
[La] (mmol.L ⁻¹)	Raw difference	0.2 ± 0.8	-0.1 ± 0.8	0.2 ± 0.6	0.0 ± 0.7	0.4 ± 0.3	0.7 ± 0.7	0.5 ± 0.4
	ES ± 90% C.I.	0.17 ± 0.62	-0.05 ± 0.52	0.12 ± 0.49	-0.01 ± 0.41	0.21 ± 0.14*	2.33 ± 2.27‡	0.77 ± 0.64#
T_{tyl} (°C)	Raw difference	0.1 ± 0.5	0.4 ± 0.5	0.1 ± 0.6	0.0 ± 0.6	0.1 ± 0.3	0.0 ± 0.8	0.1 ± 0.5
	ES ± 90% C.I.	0.30 ± 1.43	0.77 ± 1.10	0.29 ± 1.83	0.07 ± 1.70	1.45 ± 4.84	0.00 ± 1.61	0.19 ± 1.17
RPE _{over} AU	Raw difference	-	-0.5 ± 5.8	1.3 ± 7.4	0.0 ± 4.8	-0.5 ± 1.2	-5.3 ± 8.1	-2.5 ± 3.5
	ES ± 90% C.I.	-	-0.04 ± 0.42	0.14 ± 0.86	0.00 ± 0.73	-0.08 ± 0.18	-0.61 ± 0.94	-0.43 ± 0.61
RPE _{lungs} AU	Raw difference	-	-2.5 ± 7.6	-3.0 ± 12.1	-2.5 ± 7.2	-1.8 ± 7.3	-1.3 ± 2.9	-0.5 ± 7.2
	ES ± 90% C.I.	-	-0.24 ± 0.74	-0.32 ± 1.30	-0.35 ± 1.00	-0.22 ± 0.92	-0.31 ± 0.74	-0.13 ± 1.82
Thirst AU	Raw difference	-0.5 ± 0.7	-1.5 ± 0.7	-1.5 ± 1.5	-1.5 ± 3.1	1.3 ± 3.2	-2.0 ± 2.1	-1.8 ± 2.6
	ES ± 90% C.I.	-0.63 ± 0.86	-2.18 ± 0.99‡	-1.64 ± 1.43†	-1.14 ± 2.36	-0.70 ± 1.83	-1.52 ± 1.63	-1.56 ± 2.32
TC AU	Raw difference	0.8 ± 1.1	0.5 ± 1.3	0.5 ± 0.8	0.8 ± 0.8	1.5 ± 0.7	1.5 ± 1.5	0.8 ± 0.6
	ES ± 90% C.I.	0.36 ± 0.55	0.24 ± 0.62	0.27 ± 0.46	0.44 ± 0.44*	1.34 ± 0.61†	1.89 ± 1.91	0.55 ± 0.43*
TS AU	Raw difference	0.0 ± 0.0	-0.3 ± 0.6	0.0 ± 0.0	-0.3 ± 0.6	-0.3 ± 0.6	-0.5 ± 0.7	-0.5 ± 0.7
	ES ± 90% C.I.	0.00 ± 0.00	-0.31 ± 0.74	0.00 ± 0.00	-0.36 ± 0.86	-0.31 ± 0.74	-1.22 ± 1.24	-1.22 ± 1.24
Speed (km.h ⁻¹)	Raw difference	-	0.0 ± 0.0	0.0 ± 0.5	0.0 ± 0.5	0.0 ± 0.6	0.1 ± 0.7	0.4 ± 0.5
	ES ± 90% C.I.	-	0.00 ± 0.00	-0.04 ± 0.41	-0.02 ± 0.38	0.02 ± 0.42	0.05 ± 0.46	0.24 ± 0.31

Table 8-4 Comparison between ice swilling and menthol mouth swilling on physiological and perceptual variables at each time point throughout the testing bout. Variables with confidence limits that do not cross zero are in bold. Magnitude of the effect is denoted by the following symbols *: Small; # Moderate; †: Large; ‡: Very Large.

Variable	Comparison	Pre	5 min	10 min	15 min	20 min	25 min	30 min
$\dot{V}O_2$ (ml.kg ⁻¹ .min ⁻¹)	Raw difference	-	0.7 ± 6.2	1.6 ± 6.8	1.0 ± 6.4	0.9 ± 5.9	0.7 ± 6.4	1.2 ± 6.3
	ES ± 90% C.I.	-	0.12 ± 1.05	0.51 ± 2.16	0.37 ± 2.38	0.30 ± 1.95	0.32 ± 2.79	0.66 ± 3.43
$\dot{V}E$ (L.min ⁻¹)	Raw difference	-	-1.0 ± 4.3	-0.6 ± 5.9	-2.3 ± 6.0	-5.4 ± 5.6	-9.4 ± 8.4	-6.1 ± 4.6
	ES ± 90% C.I.	-	-0.25 ± 1.05	-0.04 ± 0.39	-0.11 ± 0.27	-0.32 ± 0.33	-0.42 ± 0.38*	-0.25 ± 0.19*
HR (bpm)	Raw difference	-14.0 ± 13.6	1.3 ± 5.9	1.3 ± 4.8	-1.0 ± 1.7	-0.3 ± 6.1	-0.3 ± 3.5	-1.3 ± 5.6
	ES ± 90% C.I.	-0.72 ± 0.70#	0.11 ± 0.50	0.10 ± 0.38	-0.09 ± 0.15	-0.02 ± 0.48	-0.02 ± 0.29	-0.11 ± 0.51
[La] (mmol.L ⁻¹)	Raw difference	-0.8 ± 0.8	-0.4 ± 1.5	-0.8 ± 1.6	-0.9 ± 1.9	-1.2 ± 2.1	-0.8 ± 1.6	-0.6 ± 2.1
	ES ± 90% C.I.	-0.70 ± 0.62#	-0.29 ± 0.97	-0.60 ± 1.22	-0.55 ± 1.16	-0.60 ± 1.08	2.75 ± 5.53	-0.83 ± 3.03
T_{tym} (°c)	Raw difference	0.1 ± 0.2	0.3 ± 0.5	0.1 ± 0.6	0.0 ± 0.5	0.0 ± 0.4	0.0 ± 0.6	-0.1 ± 0.3
	ES ± 90% C.I.	0.22 ± 0.66	0.51 ± 0.93	0.22 ± 1.61	0.07 ± 1.38	0.73 ± 6.01	0.00 ± 1.20	-0.25 ± 0.63
RPE _{over} AU	Raw difference	-	0.0 ± 11.8	1.5 ± 9.3	0.8 ± 7.6	0.8 ± 7.2	-5.0 ± 6.8	-2.3 ± 2.4
	ES ± 90% C.I.	-	0.00 ± 0.86	0.17 ± 1.08	0.11 ± 1.16	0.11 ± 1.10	-0.58 ± 0.79	-0.39 ± 0.42
RPE _{lungs} AU	Raw difference	-	0.0 ± 10.7	0.8 ± 9.3	-0.5 ± 7.2	-3.0 ± 8.2	0.5 ± 4.9	-1.3 ± 5.1
	ES ± 90% C.I.	-	0.00 ± 1.04	-0.08 ± 1.00	-0.07 ± 1.00	-0.38 ± 1.03	0.13 ± 1.25	-0.31 ± 1.29
Thirst AU	Raw difference	-0.3 ± 0.6	-0.8 ± 0.6	-0.5 ± 1.2	-1.3 ± 1.8	-1.3 ± 1.8	-0.8 ± 1.1	-0.8 ± 1.1
	ES ± 90% C.I.	-0.31 ± 0.74	-1.09 ± 0.86#	-0.37 ± 1.17	-0.95 ± 1.34	-0.70 ± 0.99	-0.57 ± 0.86	-0.67 ± 1.00
TC AU	Raw difference	1.0 ± 1.0	0.3 ± 0.38	0.5 ± 2.10	0.9 ± 1.50	0.9 ± 1.80	0.9 ± 2.2	0.0 ± 1.0
	ES ± 90% C.I.	0.48 ± 0.47	0.12 ± 0.37	0.27 ± 0.88	0.51 ± 0.90	0.78 ± 1.62	1.10 ± 2.73	0.00 ± 0.70
TS AU	Raw difference	0.0 ± 1.0	-0.3 ± 1.1	-0.3 ± 1.1	0.3 ± 0.6	0.0 ± 0.0	0.0 ± 1.0	-0.3 ± 0.6
	ES ± 90% C.I.	0.00 ± 1.40	-0.31 ± 1.42	-0.31 ± 1.42	0.36 ± 0.86	0.00 ± 0.00	0.00 ± 1.16	-0.46 ± 1.18
Speed (km.h ⁻¹)	Raw difference	-	0.0 ± 0.0	0.0 ± 0.5	0.0 ± 0.5	0.0 ± 0.6	0.1 ± 0.7	0.4 ± 0.5
	ES ± 90% C.I.	-	0.00 ± 0.00	-0.04 ± 0.41	-0.02 ± 0.38	0.02 ± 0.42	0.05 ± 0.46	0.24 ± 0.31

8.4 Discussion

The aim of this investigation was to assess the effects of perceptual and physiological cooling, achieved via menthol and ice mouth swilling respectively, administered at five-minute intervals, during a 30-minute training session in trained distance runners, in hot environmental conditions (35°C). The intensity of which was fixed at a rating of perceived exertion (RPE_{legs}) that corresponded to the onset of $\geq 2 \text{ mmol.L}^{-1}$ [La], with running speed determined by the athlete throughout the exercise bout as long as RPE_{legs} remained ‘clamped’. The main finding being that menthol mouth swilling lowered oxygen consumption ($\dot{V}O_2$) by a *large* to *very large* degree in the latter two thirds of the trial, when compared to control conditions. Ice swilling induced a similarly *large* reduction in $\dot{V}O_2$ at the 30-minute time point compared to no swill; when contrasted, there were no meaningful differences between menthol and ice swilling at any time point (confidence limits overlapped zero), but $\dot{V}O_2$ was higher in the ice swilling condition at each time point. The decrease in $\dot{V}O_2$ observed due to menthol mouth swilling occurred in absence of any change in $\dot{V}E$. Taken together these findings contrast with much of the previous literature which has assessed menthol mouth swilling (Mündel *et al.*, 2006; Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016; Flood, Waldron and Jeffries, 2017; Jeffries, 2018), and contradict the model proposed by Eccles (Eccles, 2000) in which menthol application to the oral cavity induces increases in $\dot{V}E$ due to stimulation of oral cold receptors.

There are several possible explanations for the differences between this work and previously conducted research. Firstly, the athletes in the present investigation are *Performance Level 4* athletes as defined by De Pauw and Roelands (2013), in that they have a relative $\dot{V}O_{2\text{max}}$ between $65\text{-}71 \text{ ml.kg}^{-1}.\text{min}^{-1}$ suggesting that the athletes are highly trained, with previous menthol mouth swilling work being carried out on athletes with mean $\dot{V}O_{2\text{max}}$ values ranging from $52\text{-}61 \text{ ml.kg}^{-1}.\text{min}^{-1}$ (*Performance levels 2 and 3*; (Mündel *et al.*, 2006; Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016; Flood, Waldron and Jeffries, 2017; Jeffries, 2018)) and 5km personal bests ranging from 17-23min (Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016). It is highly likely that empirically fitter athletes will exhibit different responses than their lesser trained counterparts. Indeed, reductions in $\dot{V}E$ during self-paced exercise performance in the heat (35°C) compared to normothermic conditions have also been reported in cyclists with high training volumes (Périard and Racinais, 2016) and in lesser trained individuals ($\dot{V}O_{2\text{peak}} \sim 60 \text{ ml.kg}^{-1}.\text{min}^{-1}$) with a high core temperature following heat exposure (Trangmar *et al.*, 2017), albeit without a cooling stimulus applied. It is not unreasonable to suggest that

when a well-trained athlete applies a cooling strategy to the oral cavity in a compensable heat at a familiar training intensity, the stimulation of oral cold receptors may be insufficient to counter the reduction in $\dot{V}E$ brought about by the heat, as this imposes a stronger thermal signal upon the trigeminal and other dependent systems (Eccles, 1994; 2003; Eccles *et al.*, 2013; Sloan *et al.*, 1993). Although, the fact that menthol represents a more potent stimulus to this effect than ice is surprising but is supported in Chapter 7 which also found trivial changes in $\dot{V}E$ at the running speeds (16-18km.h⁻¹) in this trial following menthol mouth swilling in the heat, in similarly trained athletes.

Secondly, the previously reported increases in $\dot{V}E$ and Eccles' proposed model (Eccles, 2000) were all conducted during, or based upon, situations that were exhaustive (Mündel and D. A. Jones, 2009; Flood, Waldron and Jeffries, 2017; Jeffries, Goldsmith and Waldron, 2018) or maximal (Riera *et al.*, 2014; Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016; Riera *et al.*, 2016) in nature, unlike our investigation which was submaximal. It is important to note that Eccles' model (2000; 2013) was not developed upon exercise observations, but instead upon maximal breath-holding following oral menthol use (Sloan *et al.*, 1993), restricted breathing (Nishino, Tagaito and Sakurai, 1997) and forced cold air stimulation of the airway cold receptors (McBride and Whitelaw, 1981; Burgess and Whitelaw, 1988). As such, this model may present an incomplete explanation as to the effects menthol or other cold stimuli elicit when applied to the oral cavity during submaximal exercise, with factors such as mentholated product liking and habituation possibly playing a part, alongside more established factors such as thermal (dis)comfort, thermal sensation, and athlete fitness. However, this does not rule out the possibility for hedonic responses to be elicited by menthol application, or a perceived reduction in thirst, both of which are proposed by Eccles' model (2000; 2013) and are supported elsewhere in the thesis (Chapters 6 and 7; (Best, Spears, *et al.*, 2018), although not conclusively by this investigation (Figure 8.5; Tables 8.2-8.4).

An ancillary finding concerns the interaction between $\dot{V}O_2$ and the application of cooling stimuli. The athletes were much better able to regulate their % $\dot{V}O_{2max}$ over the training session when oral cooling strategies were applied, irrespective of their nature (Figure 9.2), and whilst maintaining the dRPE clamp. Application of menthol and ice showed a range of 0.5-3% and 1-5% respectively, hence the overlapping confidence intervals in Table 9.4; whereas, in the control condition this range was much larger at 3.5-9%, and was larger in all athletes, despite non-uniform changes and curves in % $\dot{V}O_{2max}$ over the session. Variability within and between $\dot{V}O_2$ is expected even in elite distance runners, as Saunders *et al.* (2004b) report a mean coefficient of variation of 2.5% at 16km.h⁻¹ and 2.4% at

18km.h⁻¹ with the smallest worthwhile changes in $\dot{V}O_2$ considered to be similar (Shaw *et al.*, 2013). Heat is known to increase the percentage of $\dot{V}O_{2max}$ utilised as exercise duration progresses (Cheuvront *et al.*, 2010) due to concomitant increases in T_{skin} and T_{core} which redistribute blood flow and in turn increase cardiovascular strain. These mechanisms have been associated with an increase in RPE but are largely central in nature. In a clamped RPE_{legs} model exercise intensity is somewhat independent of central input as it is peripheral load that is clamped and as such governing exercise intensity/output. Given the trained nature of the participants and the personalised and submaximal nature of the exercise, if a cooling strategy attenuates the perception and subsequent interpretation of factors that may drive fatigue centrally, exercise intensity is likely to be better maintained, more tightly regulated, or potentially improved. This notion is again supported by the reduction in $\dot{V}O_2$ and largely stable running speeds seen with the application of cooling interventions, despite elevations in HR and [La] (Tables 8.2 and 8.3), although the magnitude of these effects is variable.

Further variability was seen within and between perceptual measures following swilling (Tables 8.2 and 8.3), specifically in the time course of the observed effects. Thirst tended to be reduced earlier in the exercise bout, in both conditions: menthol reduced thirst to a *moderate* extent five minutes into the exercise bout and again trended toward reduction towards the completion of the session; ice swilling followed a similar pattern of reduction but exerted greater effects (*large to very large*; Table 8.3) over a longer time (10 min). This is to be expected as thirst is a homeostatic drive for water ingestion and the provision of such would therefore be more appealing and successful in reducing thirst than a water mimetic such as menthol. Ice swilling also improved TC in the latter two thirds of the exercise session by a *small to large* degree equating 0.8-1.5 units, or approximating one verbal descriptor. Menthol was only effective in uniformly improving TC in the final 5 min of exercise (0.8 ± 0.6 units; *small*) again approximating one verbal descriptor. Thermal sensation was also reduced in both conditions in the latter two thirds of exercise, although not beyond *trivial* levels (Tables 8.3 and 8.4), this can be predominantly attributed to one athlete who experienced substantial increases in TS at 10 and 15 min despite menthol and ice swilling, respectively (Figure 8.2 Panels B and C). The time course of physiological and perceptual cooling's effects is an increasingly prevalent finding within the literature. Ingestion of ice slurries have been reported to improve perceptual and performance metrics and decrease T_{core} , but may display an increased T_{core} upon exercise termination (Siegel *et al.*, 2010; 2011; Schulze *et al.*, 2015), this has been termed a physiological overshoot. Similarly, Jeffries and colleagues (2018) showed that following a period of fixed work,

menthol mouth swilling or ice slurry ingestion elicited greater time to exhaustion than a placebo (Jeffries, Goldsmith and Waldron, 2018). This effect is not limited to the oral cavity as Barwood, Kupusarevic and Goodall (2018) report improved TS, TC and TTE employed repeated topical spraying of menthol, employing a similar design (Barwood, Kupusarevic and Goodall, 2018).

Despite the above variability across perceptual thermal measures it is hypothesised that strategies that attenuate the perception of peripheral load in the heat, as expressed by RPE_{legs} , may provide little relief in trained runners as they are likely accustomed to localised mechanical and metabolic stress associated with prolonged exercise of a relatively high intensity. Indeed, the high training volumes typically employed by elite distance runners may serve to ‘dampen the signal’ and suppress a large percentage of interpretation of mechanical or metabolic stress in working musculature, even if this is potentially injurious. Furthermore, there is limited scope beyond pouring water (Armstrong *et al.*, 2016; Morris and Jay, 2016) or applying a wet sponge (Pugh, Corbett and Johnson, 1967; Gisolfi and Copping, 1974) to affected areas in typical race scenarios. Benefits of such strategies are minimised due to the skin wettedness of athletes performing in the heat (Armstrong *et al.*, 2016), especially in humid environments, and may accelerate the predisposition to dermatological injury (Eiland and Ridley, 1996; Mailler, 2004; Mailler-Savage and Adams, 2006), especially in longer duration events such as the marathon.

A further critique of the perceptual thermal variables assessed within this study that is amplified by the small sample size is the sensitivity of the scales used to assess TC and TS. Thermal comfort is assessed with a minor improvement in sensitivity, relative to TS, as it employs a 10-point as opposed to 8-point scale. The present scales (Zhang *et al.*, 2004) were chosen due to their bidirectional nature, in that negative values are ascribed to decreases in perceived comfort and temperature and vice versa, increasing the ease of interpretation by research participants. The accompanying verbal anchors are useful too, especially when assessing TC (+0: Just comfortable; -0: Just uncomfortable), but participants tend to gravitate toward whole numerical anchors (Greenstein and Velazquez, 2017), as evidenced in Figures 9.3 and 9.4. Relevant to exercise science, evidence suggests participants typically focus more upon their semantic interpretation of the numerical anchor as opposed to the verbal descriptor (Greenstein and Velazquez, 2017) i.e. ‘What does a 5 feel like to me?’. The lack of sensitivity can be countered when assessing exercise intensity by utilising the CR100 as opposed to the CR10 scale (E. Borg and G. Borg, 2002; E. Borg *et al.*, 2009), providing a more graded but interchangeable assessment of RPE.

The CR100 has been used successfully in differential approaches to date (E. Borg and G. Borg, 2002; E. Borg *et al.*, 2009; McLaren *et al.*, 2016; 2018), hence our adoption of the CR100 in this investigation, but the development of a similar scale for assessing other perceptual and exercise-limiting variables such as TC and TS may be beneficial. Especially in well trained athletes, who typically display a reduced CV in performance (Hopkins and Hewson, 2001; Paton and Hopkins, 2005; 2006) and thus when assessing associated perceptual responses lower change scores may produce performance effects that are practically valuable, hereby reducing the smallest worthwhile change(s) in these metrics.

The duration and intensity of the exercise bout in the present study also require refinement. Both variables were selected in consultation with the athletes' coach and were based upon their current phase of training and perceived capabilities. Whilst this coach engagement ensured high levels of ecological validity, increasing the intensity of the exercise bout by one verbal descriptor (*Somewhat Hard* to *Hard*) and in turn providing a higher anchor of RPE_{legs} (~50 AU) may have led to a more appropriate 'session' intensity, that was still in the range of the athletes' aerobic threshold (Mann, Lamberts and Lambert, 2013), but may have stretched their capabilities to a greater extent than the present prescription. Similarly, increasing the session duration to 45 or 60 min, would likely have still allowed the present or adjusted intensity to be maintained, as in trained athletes it is noted that this corresponds with the pace and physiological milieu that is capable of being sustained for a marathon (Sjödín and Svedenhag, 1985; A. M. Jones, 2006), and as such exercise durations greater than two hours. These modifications may have provided an exercise stimulus than was more representative of competitive running, increasing the specificity of the session, but also more closely corresponding to the body of menthol mouth swilling literature published to date. This would have allowed for a more direct comparison between studies, and better highlighted the novel results obtained in this investigation. However, it is acknowledged that the control over athletes' training and repeated access to a group of trained athletes are luxuries afforded to this study.

To conclude, menthol mouth swilling may present a feasible and practical alternative to ice slurry swilling during exercise of 30min, in hot environmental conditions in trained runners, although a larger sample size is required to confirm these results. Menthol mouth swilling may bring about beneficial reductions in $\dot{V}O_2$ during submaximal running, potentially due to hedonic mechanisms, however these sensations do not directly manifest as reductions in TC, TS or thirst at the present sample size and employing the current forms of assessment, as such a further exploration as to athletes' qualitative perception of

menthol mouth swilling is warranted. The timing of cooling application, perceptual or physiological, in the exercise bout is also a valid consideration for future research but it is noted that menthol mouth swilling is a of greater value logistically and practically than the provision of ice swills during exercise.

CHAPTER 9 : ATHLETE EVALUATIONS OF MENTHOL MOUTH SWILLING

9.1 Introduction

There is a distinct lack of menthol mouth swilling research in applied settings with the work of Riera and colleagues the only possible exceptions to date (Riera *et al.*, 2014; Tran Trong *et al.*, 2015; Riera *et al.*, 2016). Whilst this thesis has aimed to employ an applied approach to data acquisition, consulting with athletes' coaches and opting for ecologically valid running speeds (Chapter 7) and individualised intensities corresponding to physiological landmarks (Chapter 8), the paucity of 'real world' menthol mouth swilling research persists. This absence limits the knowledge we have regarding athletes' implementation of menthol containing strategies outside of the laboratory, and their perceptions of the potentially ergogenic strategy. Prior to commencing future applied research, the perceptions of the athletes who have participated in research to date are important to consider, as their reflections may hold key insights into the strategy with respect to application and likely uptake in external competitive or training environments. Hence, this chapter aims to capture the qualitative experiences of the athletes who participated in the research described in chapters 7 and 8.

9.2 Materials and Methods

Participants from previous investigations were asked to provide verbal feedback on testing design and experiences when cooling down, following testing sessions (Reflection). Feedback, if expressed, was recorded alongside physiological and subjective data from each testing session and so was not limited to menthol solution or testing design, but may have further reflected how the athlete felt during the testing bout(s). Brief post-task interviews were used to capture the experiences of those who had participated in the running research conducted throughout this thesis. Interviews were conducted either via FaceTime, Skype or Facebook.

9.2.1 Participants

Five male participants (Age 20.8 ± 4.3 ; 5km personal best $15:43 \pm 0:26$) were recruited from previously conducted research for the reflection portion of the investigation.

9.2.2 Interview Questions

Each interview was conducted with no other participant present, either through a FaceTime or Skype call, or the Facebook messenger function. Participants were asked six questions, with questions grouped into three themes: Menthol experiences, Ecological application of menthol and General Feedback. The inclusion of General Feedback allowed for feedback obtained following testing sessions to be analysed alongside data obtained via post-task interviews. Question order was consistent between participants, due to the logical sequencing of questions posed. The questions were as follows:

1. How did you feel when using the menthol?
2. How does it compare to other strategies you currently use in training or racing?
3. Would you be open to using menthol mouth-swilling outside of the lab?
4. Are there any drawbacks to using menthol mouth-swilling?
5. Would you recommend menthol mouth-swilling to other athletes?
6. Have you anything else to add about your experiences?

9.2.3 Coding and analytical approach

Each data item was given equal attention during coding and thematic analysis as per recommendations by Braun and Clarke (Braun and Clarke, 2006). Spelling and other grammatical inaccuracies are included. Typically, such inaccuracies would be denoted with [sic], however inaccuracies are left *in situ* to best represent the individual communication styles of the participants.

9.3 Results

Four of the five participants responded to the invitation to be interviewed to obtain feedback. Participant study involvement and corresponding chapters are also stated (Table 9.1). Two of the four participants provided no comment for question 6 (Have you anything else to add about your experiences?). Table 9.1 details participants' responses to all questions for completeness; three key themes were identified and are interpreted below:

Table 9-1 Participant involvement and responses to questions pertaining to menthol mouth swilling during research and the potential for subsequent ecological application. Responses are verbatim, as such any spelling errors are attributed to the participant and not the author. RE: Running Economy; Chapter 7. Tempo: Simulated training session; Chapter 8. NR: No response provided.

Participant: LGT	Study Involvement: RE
Question	Response(s)
<i>How did you feel when using menthol?</i>	‘Felt really good using the menthol, felt was easier to breathe and run and opened up the airways which made running feel easier and more comfortable’
<i>How does it compare to other strategies you currently use?</i>	‘The only other aid I use is protein shakes just for recovery. There is nothing I do or use pre race to try and aid performance but using the menthol I felt a big difference to what I’ve been used to.’
<i>Would you be open to using menthol mouth swilling outside of the lab?</i>	‘Without doubt i would love to use the menthol outside of the lab in a natural environment.. It felt like it aides performance and would be fascinated to use it in a race and im sure it would aid the race as well.’
<i>Are there any drawbacks to using menthol mouth-swilling?</i>	‘No drawbacks at all.. It is quick, easy to use and very effective.. Aslong as enough or it is made and can be stored and transported to a race there are no issues at all.’
<i>Would you recommend menthol mouth-swilling to other athletes?</i>	‘I would deffinatly recommend it to other athletes (Maybe not my nearest rivals as id like the edge over them in using it) But id happily encourage other people to try and use it and see the difference that it has.’
<i>Have you anything else to add about your experiences?</i>	‘Reminded me in a way of using airways chewing gum in terms of opening up the airways and making breathing a lot easier. However wasnt as overpowering as airways in a good way and was much easier to breathe without that minty taste in the mouth and through the nose! Overall just made running feel a lot easier.
Participant: DN	Study Involvement: RE; Tempo
Question	
<i>How did you feel when using menthol?</i>	Felt hydrated without having to take water on which benefited me as i get stitches when taking water, so felt good
<i>How does it compare to other strategies you currently use?</i>	Ice was too sensitive for me and was more of a pain to use, using nothing didn't benefit me so the menthol was the better of the 3
<i>Would you be open to using menthol mouth swilling outside of the lab?</i>	Yes

<i>Are there any drawbacks to using menthol mouth-swilling?</i>	No, I thought it worked well
<i>Would you recommend menthol mouth-swilling to other athletes?</i>	Yes
<i>Have you anything else to add about your experiences?</i>	I think it's a good idea to use just before a race as it made me feel better just before a 5k I did, i think it would be useful during 10ks/half marathons instead of taking water on for athletes like me who struggle to use water without getting stitches or anything
Participant: HA	Study Involvement: RE; Tempo
Question	
<i>How did you feel when using menthol?</i>	I felt that with the menthol the feeling of freshness remained in my mouth for longer than with just water. However, as it was spat out I didn't quite feel that it cooled then back of my throat as well as water.
<i>How does it compare to other strategies you currently use?</i>	As the menthol only has to be swilled I feel that it is advantageous to water as you are not adding extra fluids into your system which are felt moving about.
<i>Would you be open to using menthol mouth swilling outside of the lab?</i>	If the menthol swill was easy to administer I'd use it outside of the lab.
<i>Are there any drawbacks to using menthol mouth-swilling?</i>	As mentioned, due to not swallowing the menthol solution, the back of my throat didn't still dried out.
<i>Would you recommend menthol mouth-swilling to other athletes?</i>	I'd recommend the menthol swill to other athletes
<i>Have you anything else to add about your experiences?</i>	NR
Participant: HBT	Study Involvement: RE; Tempo
Question	
<i>How did you feel when using menthol?</i>	felt like it opened my airways a bit
<i>How does it compare to other strategies you currently use?</i>	If I ever have asthma symptoms I always have ginger to open my airways up as it contains anti-inflammatory agents and I really feel the difference after. I feel that menthol has similar properties.
<i>Would you be open to using menthol mouth swilling outside of the lab?</i>	Yes

<i>Are there any drawbacks to using menthol mouth-swilling?</i>	No
<i>Would you recommend menthol mouth-swilling to other athletes?</i>	Yes
<i>Have you anything else to add about your experiences?</i>	NR

9.3.1 Menthol experiences

The subjective reports of the athletes involved in this study exemplify common responses to menthol exposure with associated mechanisms also mentioned. The most common experience is that of nasal patency or openness and is reported in 50% of respondents; athletes also mentioned feelings of freshness (HA) and thirst satiation (DN). One athlete (DN) also reported the potential for menthol to be used prophylactically to counter the possible onset of exercise associated transient abdominal pain (stitch), although this comment was not independent of comment regarding thirst satiation, the potential for menthol to be used as an alternative to counter GI symptoms was noted by another athlete as well (HA).

‘As the menthol only has to be swilled I feel that it is advantageous to water as you are not adding extra fluids into your system which are felt moving about.’

HA (2016)

When asked how menthol compares to other strategies currently employed by the athletes there was no consensus in responses, and a range of time points discussed; the above quote was provided in response to this question. One athlete commented upon the use of another botanical ingredient to counter respiratory issues (specifically, ginger for asthma treatment). The use of protein supplementation post-exercise, but absence of a pre-competition nutritional strategy was noted by another athlete (LGT), whom also stated they felt menthol may be ergogenic with respect to their performance. The remaining respondent referenced their involvement in the research, stating menthol was preferable in comparison to ice swilling, as this presented issues regarding oral sensitivity and practicality, but also that a control had no effect on performance.

9.3.2 Ecological application

All athletes responded positively when asked if they would be open to implementing menthol mouth swilling outside of the confines of the lab. Responses ranged in length from a brief ‘Yes’ (50% of respondents) to more eloquent and enthusiastic replies: HA pragmatically stated:

‘If the menthol swill was easy to administer I’d use it outside of the lab.’

HA (2016)

LGT seconded this willingness for ecological application, and provided more insight into his motivation for doing so:

‘Without doubt i would love to use the menthol outside of the lab in a natural environment.. It felt like it aides performance and would be fascinated to use it in a race and im sure it would aid the race as well.’

LGT (2016)

Interestingly, all athletes reported minimal if any negative feelings towards menthol mouth swilling with 50% of participants simply responding ‘No’ when asked if they foresaw any issues with menthol mouth swilling. The remaining respondents agreed that there were limited negative outcomes but raised points concerning transport (LGT) and the potential to ingest the swill, with a view to alleviating dry mouth (HA). One athlete (DN) subsequently provided quite a detailed overview of the potential competitive distances that menthol mouth swilling may prove to be useful, suggesting events ranging from 5km – 21.1km (half-marathon), especially if athletes have a prior history of GI distress or difficulty hydrating during exercise.

9.3.3 Other considerations

As with the ecological application of menthol, participants responded unanimously that they would recommend menthol mouth swilling to their fellow runners, with one athlete joking he wouldn’t recommend it to his nearest competitors:

‘I would deffinatly recommend it to other athletes (Maybe not my nearest rivals as id like the edge over them in using it) But id happily encourage other people to try and use it and see the difference that it has.’

LGT (2016)

Two athletes provided further detail on their thoughts regarding menthol mouth swilling, with one athlete (LGT) focusing on ecological application (reported in 9.3.2), and the other referring to a well-known menthol containing chewing gum as a comparison:

‘Reminded me in a way of using airways chewing gum in terms of opening up the airways and making breathing a lot easier. However wasnt as overpowering as airways in

a good way and was much easier to breathe without that minty taste in the mouth and through the nose! Overall just made running feel a lot easier.’

LGT (2016)

9.4 Discussion

The aim of this investigation was to capture the reflective accounts of the athletes who participated in the research undertaken in Chapters 7 and 8 of this thesis. The intention being to ascertain whether menthol mouth swilling would be an acceptable ergogenic strategy beyond the confines of the laboratory, and elucidate participants’ perceptions of how this may be achieved, along with any further factors participants wished to raise. To this end, three key themes emerged: Menthol experiences, ecological applications and other considerations. The remainder of this discussion will place these findings in the context of supplement use and beliefs within the athletic population, placebo and nocebo effects, and potential future applications of menthol mouth swilling based upon athlete recommendations.

Product use is considered to be governed by a user’s perception of the product, and not objective reality of the product’s attributes (Mason and Bequette, 1998). Mason and Bequette (1998) proffer a pertinent example of this in that consumers use bad tasting mouthwash due to the perception that more bacteria are treated. This trade-off is described as an attribute covariance perception (Mason and Bequette, 1998), but can also be considered as an assessment of hedonic and utilitarian attitudes (Batra and Ahtola, 1991). Batra and Ahtola (1991) describe these factors as an assessment of a product’s sensory affect, and ‘expectations of consequences’.

This bi-dimensional cost-benefit approach is of use to sport and exercise scientists as an effective intervention may be heavily weighted towards the utilitarian component, but the absence of a hedonic aspect means that there is reluctance in implementation. An example of this may be (high dose) sodium bicarbonate or beta-alanine; each supplement is underpinned by sound theory, and target established physiological mechanisms that are known to limit performance, but are associated with gastrointestinal symptoms and paraesthesia, respectively (Maughan *et al.*, 2018). These unpleasant experiences score poorly for hedonic value and may limit implementation. Conversely, factors that tend to increase hedonic value may be of little utilitarian consequence. There are multiple examples of this effect in consumer literature, but common examples are wine (Wiedmann and Hennigs, 2012 p. 381; Wolf, Morrish and Fountain, 2016) and luxury goods (Hagtvedt and Patrick, 2009; Husic and Cicic, 2009), where products with high hedonic value are

perceived to be more desirable but ultimately perform the same function. Returning to sports science, effective supplementation strategies exemplify hedonic and utilitarian components: Hurst *et al.*, (2017a) provide a worked example where an athlete uses a supplement for the first time and attributes any performance improvement to the supplement, increasing the likelihood of future use, and potentially influencing the efficacy of that supplement within that athlete through a form of Pavlovian conditioning (Everitt and Robbins, 2013; Hurst *et al.*, 2017).

Performance enhancement satisfies both hedonic and utilitarian needs for athletes, but the hedonic component can be further enhanced by manipulating factors such as active ingredients (de Araujo *et al.*, 2012) colour (de Craen *et al.*, 1996; Szabo *et al.*, 2013; Best *et al.*, 2018), taste (de Araujo *et al.*, 2012; Verastegui-Tena, van Trijp and Piqueras-Fiszman, 2018), and mode of administration (Szabo *et al.*, 2013). As such if a practitioner wishes to enhance performance through administration of a sound utilitarian intervention, the intervention can be improved upon by tending to these hedonic factors. These effects may extend to placebo and nocebo treatments (Kong *et al.*, 2013; Petersen *et al.*, 2014), so care must be taken when designing these arms of supplement trials too.

This balance is best exemplified by the second quote in section 9.3.2, which although focuses on the ecological application of menthol specifically states a perception of performance enhancement. The same athlete had also previously described how menthol balanced hedonic and utilitarian needs (LGT, 206; Table 9.1): ‘Felt really good using the menthal [sic], felt was easier to breathe and run and opened up the airways which made running feel easier and more comfortable’. These are classic menthol perceptual responses (Eccles, 1994), that have also been documented to confer a hedonic effect (Eccles, 2000; Eccles *et al.*, 2013).

Athletes also recommended using menthol prophylactically to counter gastrointestinal issues (10.3.3 *Other considerations*), which commonly affect a large percentage of competitive runners across a range of distances (Pfeiffer, Stellingwerff and Hodgson, 2012; de Oliveira, Burini and Jeukendrup, 2014; Costa *et al.*, 2016; Costa, Hoffman and Stellingwerff, 2018). This was attributed to countering the onset of a stitch (DN), and to avoid drinking an excessive amount of water (HA). Both of which would likely have detrimental effects upon performance (Pfeiffer, Stellingwerff and Hodgson, 2012; Stuempfle and Hoffman, 2015; Hew-Butler *et al.*, 2015). Interestingly, menthol has been associated with a reduction of gastrointestinal symptoms due to TRPM8 channels acting as a possible drug target (Holzer, 2011). So, there may be a mechanistic basis to the rationale of menthol supplementation to reduce gastrointestinal symptoms, especially if

one were to swallow the swill as recommended by one of the athletes in section 9.3.1; *Menthol experiences*. However, hydration status of the athlete, event duration and environmental conditions should be considered if the sole purpose is to reduce the volume of water to be consumed during an event, as menthol consumption may attenuate thirst as per Chapter 5 and Eccles' recommendations (Eccles, 2000; Eccles *et al.*, 2013).

To conclude, menthol mouth swilling is a strategy that presents a blend between hedonic and utilitarian components of product attribution in the population that was involved in the research throughout this thesis. Further work is needed to elucidate if these effects remain outside of the laboratory, but there is a clear desire by athletes for this work to be completed and for menthol mouth swilling to be as accessible and effective strategy as possible.

CHAPTER 10 : SYNTHESIS OF FINDINGS

10.1 Restatement of aims

This thesis aimed to develop a mentholated solution to impart sensations of perceptual cooling, during endurance exercise performance, in trained middle and long distance runners at intensities representative of training and competition. The effects of swilling this solution were compared to that of other ergogenic strategies, in hot environmental conditions.

Expressly, the preferred concentration of menthol within a mentholated mouth swill was derived (Chapter 5; Best, Spears *et al.*, 2018); the preferred colour of this solution was also determined, with a view to maximising the perceptual cooling characteristics of the solution by taking advantage of sensory associations and expectancy of ‘cool’ products.

The mentholated mouth swill was then compared to 10% carbohydrate and control swills, at rest, in hot environmental conditions (35°C and 10% humidity; Chapter 6) and participants’ physiological and perceptual responses assessed at three minute intervals throughout.

This initial resting experiment was followed by two exercise trials in Chapters 7 and 8. The first trial (Chapter 7) aimed to determine the effects of mentholated mouth swilling upon ventilatory, physiological, performance and perceptual responses when administered at typical training and competitive intensities (14 – 20km.h⁻¹ + 1km time trial), in temperatures pertinent to British middle and long distance runners (14°C and 28°C). The second trial (Chapter 8) again assessed the ventilatory, physiological and perceptual responses of athletes during exercise, but assessed these parameters during a simulated training session which consisted of 30-minutes at a fixed rating of perceived exertion, (RPE_{legs} corresponding to the onset of ≥ 2 mmol [La]) in hot environmental conditions (35°C and 10% humidity). Menthol mouth swilling was compared to ice swilling, thus comparing perceptual and physiological cooling strategies.

Finally, Chapter 9 aimed to capture participants’ feedback on menthol mouth swilling during exercise and capture their thoughts on the potential for application outside of the laboratory either in training or competition (Chapter 9).

10.1.1 Principle findings

This section details the principle findings of the thesis, on a per chapter basis, progressing through Chapters 3 – 9.

The thesis proper, began by assessing and quantifying the magnitude of and accompanying uncertainty within performance changes brought about by topical and ingested cooling strategies (Chapter 3; Best, Payton *et al.*, 2018). The relationship between the timing of cooling strategies around an exercise bout and exercise performance was also determined, with a combination of pre and percooling shown to be most effective i.e. cooling before and during the event in combination. Menthol containing strategies that were ingested prior to and during the exercise bout produced the largest effects upon performance in this meta-analysis (Best, Payton, *et al.*, 2018).

Due to the menthol content within the cooling strategies that demonstrated the greatest ergogenic effect upon time trial performance (Chapter 3; Best, Payton *et al.*, 2018), the role of different modes of menthol administration upon exercise performance were further scrutinised (Chapter 4; Stevens and Best, 2017). Menthol has been applied orally and topically during exercise, with most evidence suggesting a greater ergogenic potential when used as a mouth swill or within other fluids during endurance activity, thus supporting the findings of Chapter 3. Lesser effects are observed when applied topically, especially with respect to muscular function and force production (Chapter 4; Stevens and Best, 2017).

Differences in menthol concentration of oral application strategies were also noted as part of the systematic review presented in Chapter 4 (Stevens and Best, 2017), hence Chapter 5 (Best, Spears, *et al.*, 2018) established the preferred concentration of menthol within a mouth swill to be utilised in subsequent investigations. Concentrations of 0.095% and 0.105% were seen to be more highly rated than other solutions with respect to total solution score (Chapter 5; Best, Spears, *et al.*, 2018). Colour preference was also included in this investigation, as this has been shown to influence product experience, and may enhance the ergogenic properties of menthol mouth swilling when administered by clinicians or practitioners. In addendum to the published work presented in Chapter 5 (Best, Spears, *et al.*, 2018), further analysis of the constituent components of total score by multiple regression found that participants rated solutions more highly if they were deemed more pleasant, with respect to irritation and mouth feel. This suggests that participants value a solution that is well tolerated, as opposed to being highly rated for taste, smell or freshness. The physiological and perceptual responses to the preferred swill were then compared to carbohydrate in a hot environment at rest (Chapter 6). Small increases in heart rate were observed after carbohydrate and water swilling, with moderate differences in T_{tym} between control and all testing blocks. When swilled, menthol improved TC by a small extent relative to carbohydrate and water, also moderately reducing TS and thirst when

compared to the other experimental conditions. These effects persisted when dietary carbohydrate intake of the participants were controlled for via MANCOVA.

Chapter 7 examined responses to menthol mouth swilling at typical training and competitive intensities in cool (14°C) and hot (28°C) conditions, in trained distance runners ($\dot{V}O_{2\max} > 60\text{ml.kg}^{-1}.\text{min}^{-1}$). Responses across all perceptual and physiological measures showed a high degree of inter-individual variability, but $\dot{V}E$ tended to increase following menthol swilling in the heat, with a large decrease in RPE_{over} observed following the conclusion of a 1km time trial in the same condition. This apparent improvement cannot be attributed directly to menthol due to a more conservative pacing strategy being adopted. When compared to a physiological cooling strategy in Chapter 8, menthol mouth swilling showed potentially advantageous decreases in $\dot{V}O_2$ as athletes progressed through the fixed intensity exercise bout. This change in oxygen consumption occurred in the absence of changes in $\dot{V}E$, T_{tymp} and $dRPE$. Physiological cooling by ice swilling, elicited a more rapid (TC) or greater magnitude (thirst) of change in perceptual variables, when compared to a control than menthol. However, menthol also demonstrated moderate reductions in thirst at the start of the exercise bout and improved TC at the end of the exercise bout, suggesting that menthol mouth swilling may be a more practical on course or in training solution in the absence of availability of physiological cooling agents.

Finally, to conclude the thesis, qualitative reflections from participants were captured to document their experiences of menthol mouth swilling during exercise and assess the potential ecological application of menthol mouth swilling in athletic populations (Chapter 9). Menthol mouth swilling was considered a balance hedonic and utilitarian components of product attribution in a potential target population of athletes. It is unclear whether these positive effects remain outside of laboratory settings, but there is a strong desire by athletes for such applied work to be conducted and for menthol mouth swilling to be accessible.

10.2 General Discussion

10.2.1 Training and competitive implications

The following section will outline the scope of menthol mouth swilling in specific training and competitive scenarios. This discussion will be limited to the context in which menthol mouth swilling will be employed, as opposed to the practicalities of delivering within these environments, which are discussed subsequently.

10.2.1.1 Menthol as a supporting strategy during heat acclimation

Previous research has shown menthol mouth swilling to acutely improve time to exhaustion (Mündel and D.A. Jones, 2009; Flood, Waldron and Jeffries, 2017; Jeffries, Goldsmith and Waldron, 2018) and time trial performance (Riera *et al.*, 2014; Tran Trong *et al.*, 2015; Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016; Riera *et al.*, 2016). Similarly, pre-and percooling strategies may also improve exercise performance in the heat (Stevens, Taylor and Dascombe, 2016; Best, Payton, *et al.*, 2018) when applied for a single (Marsh and Sleivert, 1999; Quod *et al.*, 2008; Duffield *et al.*, 2010) or between bouts of exercise (Tran Trong *et al.*, 2015; Galpin *et al.*, 2016; Chan *et al.*, 2017). Little is known, however, about how these strategies can be implemented in training alongside a heat acclimation protocol or training camp. The use of pre-and percooling strategies to support key, but not all, sessions within a heat acclimation protocol or training camp may allow for either a greater training duration or intensity, or a greater time at an elevated core temperature. This extended exposure to heat stress may provide further adaptations that would otherwise not have been attainable by the athlete, as sufficient time under heat stress may not have been attained, or may have come with an increased cost e.g. a compensatory adjustment in subsequent training sessions or the onset of heat illness.

Ecologically, the use of menthol mouth swilling in a laboratory-based acclimation programme would be easy to administer, and monitor the effects of administration upon performance, underpinning physiological adaptations and subjective outcomes. Variation in training session stimulus throughout the acclimation protocol would also allow for further exploration into the efficacy of menthol mouth swilling in the heat. Likewise, if one were to employ menthol mouth swilling over the course of a heat training camp, it would be prudent to target long runs, where increased heat storage is a product of exercise duration i.e. greater opportunity for heat accumulation. Interval sessions that allow for regular, repeated aliquots of the mouth swill to be utilised such as in Chapters 7 and 8 would also be sensible choices. Within these sessions an increase in heat storage is likely due to increased metabolic heat production (Mora-Rodriguez, Del Coso and Estevez, 2008), as exercise intensity and anaerobic contribution is greater (Febbraio *et al.*, 1996), coupled with a decrease in evaporative heat loss (Kenny *et al.*, 2009; Kenny and Jay, 2013), and lowered skin blood flow (González Alonso, Crandall and Johnson, 2008; Crandall and González-Alonso, 2010). Interval sessions would also account for the potential for menthol to attenuate sensations of breathlessness, or increased RPE_{lung} brought about by high intensity running, as per Chapter 7.

Menthol mouth swilling may also be a useful addition to adjunct heat acclimation strategies such as hot water immersion (Zurawlew *et al.*, 2016; Zurawlew, Mee and Walsh, 2018), or the wearing of additional clothing (Stevens, 2018), where the treatment elicits either a heat maintenance (hot water immersion) or heat storage (additional clothing) response. In these instances, as is often reported during exercise, menthol may serve to ameliorate thermal comfort and sensation, again extending the time for which an athlete is exposed to the adaptive stimulus. Whether using menthol directly to support heat acclimation, or to support adjunct strategies, care must be taken to monitor athletes for signs of heat illness, or increased physiological strain that does not return to normal upon sufficient recovery, as the possible negative effects of extended or repeated heat exposure following perceptual cooling (i.e. menthol) is not currently known (Stevens and Best, 2017; Best, Payton, *et al.*, 2018).

10.2.1.2 Ultra-endurance activity and gastrointestinal upset

Approximately 30-50% of endurance athletes experience gastrointestinal issues (de Oliveira, Burini and Jeukendrup, 2014), and typical estimates in ultra-endurance athletes are >60% (Gaskell, Snipe and Costa, 2019), with incidences as high as 93% reported (Jeukendrup *et al.*, 2000) following an Ironman™ triathlon. There is also variability of prevalence reported between training and competition (Pugh *et al.*, 2018), and the potential for differences in onset of gastrointestinal symptoms between exercise modalities (Pfeiffer, Stellingwerff and Hodgson, 2012; Costa *et al.*, 2017). Prevalence also increases with exercise intensity and duration (Pfeiffer *et al.*, 2012; Costa *et al.*, 2016; 2017), and may be further exacerbated by the heat (Glance, Murphy and McHugh, 2013; Guy and Vincent, 2018), due to factors such as translocation of lipopolysaccharides potentially inducing endotoxemia (Guy *et al.*, 2016). Attenuating these symptoms through mentholated product ingestion would likely improve training time and intensity and reduce race attrition. Menthol mouth swilling may also allow for a welcome break from carbohydrate ingestion or swilling towards the end of non-ultra-endurance events, or respite from carbohydrate dominant strategies in ultra-endurance activity, where flavour fatigue may be considered a limiting factor (Costa *et al.*, 2014; Costa, Hoffman and Stellingwerff, 2018).

Menthol ingestion, in some form, may also warrant consideration in long or hot events where gastrointestinal injury is a likely side effect of participation. Peppermint is commonly used to treat gastrointestinal symptoms, and has been shown to be effective in the alleviation of symptoms related to irritable bowel syndrome (Kline *et al.*, 2001; Ford

et al., 2008; Alammari *et al.*, 2019), and to a lesser extent reduce nausea (Tate, 1997; B. Lane *et al.*, 2012), colonic tension (Shavakhi *et al.*, 2012), and flatulence (Kline *et al.*, 2001). Peppermint may also improve rate of gastric emptying (Inamori *et al.*, 2007). These findings suggest that the administration of menthol, which is a natural derivative of peppermint oil, may have potential therapeutic benefits that may be useful for athletes that suffer with gastrointestinal issues (Holzer, 2011), and extend beyond the stimulation of TRPM8 receptors as a mediator of cold temperature detection (Bautista *et al.*, 2007; Gavva *et al.*, 2012). Ginger has previously been used to mitigate gastrointestinal issues in elite ultra-marathon runners (Stellingwerff, 2016), suggesting a consumer appetite for natural or plant based strategies in this population.

10.2.2 Practical implications

There are several practical implications elucidated by the research conducted in this thesis, that should be borne in mind if menthol mouth swilling is to be implemented outside of the confines of a laboratory by practitioners, or to further strengthen experimental design.

10.2.2.1 Individual variation in menthol preference

Individual variation in menthol preference may be a predictor in assessing an athlete's response to menthol mouth swilling. In Chapter 5, no statistically significant differences between participants' ratings of menthol concentrations were found, but *small* standardised differences in means were noted. Visually, elevations in VAS rating seem to appear at low, medium and high menthol swill concentrations (see Figure 5.1A), hinting at the possibility of thresholds for menthol liking; these thresholds may have been more apparent had fewer solutions been assessed. Similarly, the addendum to Chapter 5 highlights that participants respond to the solution that causes the least irritation and has the most pleasant mouth-feel.

Physiological and cultural differences are two plausible explanations for the emergence of menthol liking thresholds within the data set. Physiologically, this variation may be explained in part by genetic factors relating to the expression of TRPM8 receptors (Morgan, Sadofsky and Morice, 2015), the sensitivity of their trigeminal nerve (Viana, 2011; Frasnelli *et al.*, 2011; Michlig *et al.*, 2016), and one's ability to differentiate between trigeminal stimuli (Cliff and Green, 1996; Frasnelli *et al.*, 2011), as well as the thickness of the stratum corneum in the area under menthol exposure (H.R. Watson *et al.*, 1978). Whereas cultural differences may dictate factors such as menthol concentration within products, and in doing so expose an individual to a higher or lower concentration of

menthol acutely or chronically if one is a habitual consumer, which in itself can alter sensitivity to menthol (Kalantzis, Robinson and Loescher, 2007; Patel, Ishiuiji and Yosipovitch, 2007; Klein *et al.*, 2010; Botonis *et al.*, 2016). The role and time course of habituation to menthol at an individual level has practical implications upon an athlete, or practitioner, aiming to assess menthol mouth swilling in training, with a view to implementing in competition. This may mean purposefully withholding menthol containing stimuli from their diet, or not using menthol mouth swilling in selected sessions to deliberately increase subjective factors such as thermal discomfort and sensation.

10.2.2.2 Interfering with hydration and thirst

In Chapter 6, it was found that menthol may mimic the effects of swilling water around the oral cavity in as much as it can reduce thirst, whilst concomitantly improving measures of thermal comfort and thermal sensation. These *small to moderate* effects remain when dietary carbohydrate intake is controlled for, which may affect the effectiveness of carbohydrate mouth swilling during exercise trials in some instances (Fares and Kayser, 2011; S. C. Lane *et al.*, 2013; Che Muhamed *et al.*, 2014), but is not entirely supported (Ali *et al.*, 2016). Chapter 6 served as a proof of concept of Eccles' model ((Eccles, 2000; Eccles *et al.*, 2013) Figures 10.2 and 10.4), in that thirst was reduced as a result of menthol stimulation of the oral cavity.

Whilst thirst is not performance limiting *per se* (Cheuvront *et al.*, 2010; Sawka, Cheuvront and Kenefick, 2015; Kenefick, 2018), the opportunity to implement a strategy that attenuates thirst at a lower weight cost than swilling from a water bottle may confer an energetic (W/kcal saved due to weight minimised) and resultant performance (time trial performance) advantage to a rider or runner.

Exercise durations of approximately one hour e.g. 40km time trial, may be a useful starting point for implementation, as they can be performed competitively with minimal need for exogenous fuelling strategies due to not entirely depleting endogenous carbohydrate stores (Fares and Kayser, 2011), and represent a relevant performance test which displays a low coefficient of variation in lab and outdoor settings (Smith *et al.*, 2001).

A natural extension of this work would be to assess the effectiveness of menthol mouth swilling upon exercise performance following graded levels of hypohydration, as this further acts as a driver of thirst (when expressed as a change in blood osmolality), as per Figures 10.2 and 10.4 (adapted from (Eccles, 2000; Eccles *et al.*, 2013). A hypohydration range of 2-4% is representative of those typically attained during training or competition

and so is recommended. This has relevance for not only elite athletes, but also recreational exercisers who have professions which may predispose them to becoming hypohdrated.

10.2.2.3 Flavour fatigue and habituation: two sides of the same coin

Flavour or taste fatigue is a concern for athletes during prolonged endurance activity, and ultra-endurance competitions. It is brought about by repetition of a flavour stimulus which in effect acutely desensitises taste receptors to a previously pleasant or tolerable flavour. In endurance sports, flavour fatigue is commonly associated with carbohydrate containing products as they are sweet, so a contrasting stimulus that, in the case of menthol, is cooling may serve to counter this, as these stimuli target and are transduced by different TRP receptors than sweet flavours (TRPM5; (Liu and Liman, 2003)). Severity and consequence of flavour fatigue can vary greatly, from a practitioner having to alter a feeding strategy to an inability for an athlete to tolerate foodstuffs, potentially leading to race withdrawal if prolonged and severe. This is also seen in menthol's counterirritant capsaicin (Karrer and Bartoshuk, 1995; Cliff and Green, 1996; Kalantzis, Robinson and Loescher, 2007).

Similarly, given menthol's increasing status as a potential ergogenic aid we must remain open to the possibility that one may become habituated to the strategy and the ergogenic potential of the stimulus diminishing, accordingly. This may be able to be predicted to a certain extent by simple questions that outline an athlete's use and preference for menthol containing or mint flavoured products. These questions may elucidate an athlete's acceptability and typical usage of menthol products; if usage remains consistent despite the introduction of menthol mouth swilling in training or competition and the athlete is still demonstrating improvements in perceptual or performance outcomes, it may be safe to assume habituation has not taken place. Conversely, if the athlete is avoiding or reducing their consumption/use of other menthol containing products, or reporting lower perceptual responses to the intervention independent of accompanying improvements in physiological markers (e.g. T_{core} , sweat rate), it may be assumed that habituation has occurred.

Habituation of thermal sensation has been observed when a moderate menthol concentration of 0.2% was applied topically over the course of a week (Gillis *et al.*, 2015). This habituation response was attributed to a pathway specific to thermal sensation, as it occurred independent of other physiological or perceptual responses (Gillis *et al.*, 2015). Similarly, habituation to sweet stimuli have been reported (Leterme *et al.*, 2008), and are attributed to gustative habituation to sweet taste, as opposed to a reduction in pleasure derived from exposure to sweet stimuli. Conversely this response is yet to be observed in

menthol mouth swilling, as evidenced in Chapter 6, wherein the elevated heart rate observed in response to carbohydrate and water swilling is explained at least in part as an anticipatory rise of heart rate brought about by expectation of hedonic stimuli. This response is absent in an acute menthol stimulus, as it is yet to be conditioned or habituated, but as responses to topical application of menthol can be habituated (Gillis *et al.*, 2015), it is reasonable to suggest that oral cold receptors can also become habituated to menthol containing stimuli, at appropriate concentrations through a similarly mediated or trigeminal pathway.

10.2.2.3 Combining function and form

Menthol, in comparison to other established sports nutrition strategies, is simply a flavour molecule that exerts some measurable physiological effects, but predominantly targets perceptual sensory cues related to temperature through stimulation of oral cold receptors (Eccles, 1994; 2000; 2003; Eccles *et al.*, 2013), mediated through TRPM8 receptors (Bautista *et al.*, 2007; Frasnelli *et al.*, 2011) and the trigeminal nerve (Eccles, 1994; Patel, Ishiuiji and Yosipovitch, 2007; Frasnelli *et al.*, 2011). Despite ‘only’ being a predominantly perceptual cooling agent, menthol has demonstrably improved performance in time trial and time to exhaustion tests. A sports science practitioner or athlete may however be reluctant to employ a menthol mouth swilling strategy as other factors such as substrate availability, hydration status or elevated core temperature may limit performance to a greater extent than impaired thermal comfort, or elevated thermal sensation. Hence, combining menthol with other ergogenic strategies that target factors that physiologically limit performance is a prudent and economical option.

Menthol has been shown to exert a temperature dependent effect upon cycling (Riera *et al.*, 2014) and triathlon (Tran Trong *et al.*, 2015) training performance when combined with physiological cooling strategies, eliciting *moderate* improvements (Best, Payton, *et al.*, 2018) when consumed before and during exercise. These findings were then challenged to some extent, by the same research group (Riera *et al.*, 2016) as when completing a 30km cycling time trial, the combination of pre and percooling with a cold beverage and menthol ice slurry respectively, evoked *trivially* slower performances (3815 ± 455 s) relative to percooling with menthol ice slurry only (3737 ± 522 s). The authors suggest that as time trial differences were not statistically significant and the combination of pre and percooling significantly ($p < 0.05$) lowered RPE during the latter stages of the time trial, that a combined cooling approach may be most useful in longer endurance events, confirming their previous findings (Riera *et al.*, 2014; Tran Trong *et al.*, 2015) *ex*

post facto. The lack of performance enhancement over the shorter time trial duration may be attributed to attaining a trigeminal sensory threshold, whereby the cold stimulus is perceived as too cold by targeting physiological and perceptual mechanisms simultaneously.

Assessing tolerance for such strategies is advised prior to implementation; overstimulation of the area neighbouring the trigeminal nerve can lead to sphenopalatine ganglioneuralgia (brain freeze) (Bird, MacGregor and M. I. Wilkinson, 1992; Hulihan, 1997; Mages *et al.*, 2017) or migraine (Viana, 2011) following aggressive cooling of the oral cavity. Such consequences may be avoided by lowering the menthol concentration of an ice slurry solution, or by increasing the water content of the slurry. There is a tendency for ice slurries to be manufactured with commercially available carbohydrate electrolyte beverages (Gatorade™; (Siegel *et al.*, 2010; 2011; M.L. Ross, Garvican and Jeacocke, 2011)). If menthol were to be included in an ice slurry, electrolytes may warrant exclusion from the solution as salt depresses the freezing point of water, potentially increasing the risk of sphenopalatine ganglioneuralgia or migraine in susceptible individuals.

Carbohydrate provision during or prior to exercise is considered ergogenic and already has a familiar association with menthol through several commercial products such as Kendal mint cake, breath-mints and fisherman's friends. There is an established body of literature showing carbohydrate ingestion (Gant, Stinear and Byblow, 2010; Jeukendrup, 2014) or swilling (Carter and Jeukendrup, 2004; Chambers, Bridge and Jones, 2009) to be beneficial to exercise performance and capacity; this benefit occurs independent of sweetness (Rollo and Williams, 2011). The rate of carbohydrate provision and thus oxidation can be increased by providing multiple transportable carbohydrates (Jeukendrup, 2010), which in turn decreases oxygen consumption and the risk of gastrointestinal upset (Stellingwerff, 2012; Best, Barwick, *et al.*, 2018). The notion of a carbohydrate and menthol mouth swill is perhaps most appealing as it combines two strategies in one bolus. Chapter 6 presented evidence to suggest that menthol can alleviate thirst, independent of carbohydrate intake, suggesting that there would be limited interference between ergogenic aids if they were to be combined into one strategy. Equally, the addition of carbohydrate may make menthol more appealing, as shown in Chapter 5, there are a wide range of menthol preferences and the possibility to further personalise this intervention by manipulating sweetness may ensure that a beneficial menthol concentration is maintained in solution, despite a personal dislike. This combined approach may be limited in its application however, as carbohydrate mouth swilling is perhaps best employed either in a fasted state (Fares and Kayser, 2011; Che Muhamed *et*

al., 2014), or when muscle glycogen stores are not considered limiting provided adequate prior nutrition e.g. 40km cycling race; half marathon. One must also consider athlete ‘buy-in’ or willingness to adopt a strategy, and it is uncertain as to whether the inclusion of carbohydrate into a menthol solution would diminish the currently documented enthusiasm for the strategy, as per Chapter 9.

Unlike carbohydrate, caffeine may not present a natural pairing with menthol. Despite being incredibly understood and an established ergogenic (Burke, 2008; Pickering and Kiely, 2017; 2018), caffeine is typically bitter (Lipchock *et al.*, 2017; Poole and Tordoff, 2017; Gramling, Kapoulea and C. Murphy, 2019) and so may counter the natural freshness associated with menthol (Eccles, 1994; Patel, Ishiuiji and Yosipovitch, 2007; Best, Spears, *et al.*, 2018). Although, there is a paucity of literature about how menthol relates to power or repeated sprint performance (O.R. Gibson, Wrightson and Hayes, 2018), and pairing menthol with caffeine may provide an additive effect to that of menthol or caffeine when applied in isolation in power based events in the heat.

The form of menthol and any ergogenic aid it is combined with warrants practical consideration too. Liquids likely are the most practical, as they can be administered at feed stations, easily transported during exercise and to events, but the potential for menthol to attenuate thirst (Chapter 6) suggests this may not always be the best option. Ice slurry presents an appealing combination when performance is physically and perceptually limited by temperature, but the strategy is accompanied by logistical and technical hurdles. Finally, a gel or gum would allow for a small dose of carbohydrate to be mentholated and easily packaged, ensuring an even load of menthol and potential fuel throughout an event, with greater control over the dose and concentration of menthol compared to the other potential forms outlined.

Ultimately the decision to combine menthol with other ergogenic strategies, or vice versa, will be dependent upon athlete preference, the rules of competition, feeding frequency available to supporting practitioners and timing relative to desired performance outcomes.

10.2.3 Research implications

Menthol mouth swilling remains a novel nutritional strategy that is potentially ergogenic in athletic populations, under certain environmental and regulatory constraints. Despite the work undertaken for this thesis and critical reflections thereafter presented above as future practical and training implications, questions pertaining to menthol mouth swilling remain. This section groups these future research questions into four key themes:

10.2.3.1 Method of dilution

Differences in menthol mouth swill preparation remain within the literature. The method employed within this thesis and published as Chapter 5 (Best, Spears, *et al.*, 2018) consists of dissolving a dose of menthol crystals (g) in a volume of ethanol so as to produce a 5% solution. This stock solution is then diluted to the appropriate experimental concentration, the colour of which can then be manipulated if desired. For the purposes of this thesis the desired concentrations ranged from 0.005 to 0.105% in Chapter 5, with a concentration of 0.1% employed during experimental trials (Chapters 6-8).

The use of an alcohol as a solvent was advised as necessary by the institute's head laboratory technician as menthol is less dense than water, at $0.89 \text{ g}\cdot\text{cm}^3$ compared to $0.997 \text{ g}\cdot\text{cm}^3$ respectively. Menthol's lesser density relative to water means that if a solvent is not used to manufacture a mentholated solution, an opaque, thin, white film forms upon the solution (personal observations) in most instances. Swilling menthol in hot environmental conditions may mitigate this limitation slightly as the temperature of the oral cavity and the environments typically investigated are similar to the melting point of the (-)-isomer of menthol ($37.78\text{-}43^\circ\text{C}$; National Center for Biotechnology Information, 2019). However, if not fully dissolved the remaining crystalline film will likely negatively impact upon the qualitative experience of menthol mouth swilling, and athletes may be less likely to employ the strategy in future. This warrants practical consideration too, if menthol mouth swills were to be commercialised an appropriate vessel and preparatory procedure would need to be developed to avoid a film forming prior to use. It is unlikely that the classic instruction 'shake well before use' would result in an even distribution of the film, and thus negatively impact upon the characteristics assessed in Chapter 5 and the accompanying addendum.

Jeffries' group describes an alternative dilution method whereby menthol and water are heated to 40°C at a 0.01% concentration, cooled then stored for up to two months (Flood, Waldron and Jeffries, 2017; Jeffries, Goldsmith and Waldron 2018). This method of dilution targets menthol's relatively low melting point as a method for dilution, and by heating menthol and water may increase the volatility of the solution, if implemented soon after the dilution, as heating generates excitation of water and menthol molecules, potentially presenting as a more potent olfactory stimulus (at least in the short term) than our method of dilution. This hypothesis is partially supported by the lower experimental concentration employed within this investigation, although the olfactory integrity of this method of dilution remains to be established and / or compared to that presented in Chapter 5. Establishing differences between dilution methods is important to ensure a consistent

menthol stimulus can be presented to an athlete during training or competition, and diluted solutions can retain their ‘freshness’ if they are to be stored or transported to events that take place over multiple days, or even weeks as may be the case for the Olympic Games, or most World Cup formats.

Other groups have utilised the same concentration of menthol as Jeffries and colleagues (Mündel and D.A. Jones, 2009; Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016; O.R. Gibson, Wrightson and Hayes, 2018), yet report a much simpler dilution procedure of crushing menthol crystals and dissolving these crystals in deionised water. The dilution is typically reported to take place in ambient laboratory conditions (Mündel and D.A. Jones, 2009; Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016; Gibson, Wrightson and Hayes, 2018), but all experimental procedures, and thus administration of menthol, took place in temperatures approaching menthol’s melting point (33-40°C (Mündel and D.A. Jones, 2009; Stevens, Bennett, *et al.*, 2016; Stevens, Thoseby, *et al.*, 2016; Gibson, Wrightson and Hayes, 2018)).

These methodological differences likely explain why no crystalline films are reported within the menthol mouth swilling literature to date, as all methods of dilution and administration directly or indirectly take place at the melting point of the isomer of menthol used for research purposes. It is worth noting that a crystalline film could inadvertently elicit a much more potent menthol stimulus than that of a mouth swill, as one would effectively be ingesting a concentrated bolus of a high percentage menthol crystal.

The need for a ‘gold standard’ menthol dilution procedure is not necessarily warranted as each method is not without its own limitations, but a comparison between methods of dilution at a matched concentration warrants investigation as they may bring about different responses to subjective measures and $\dot{V}E$, or associated respiratory measures, and may demonstrate differences in product consistency and shelf-life.

10.2.3.2 Elucidating mechanisms and expanding Eccles’ models

Figures 10.2 and 10.3 display the effects of menthol upon oral and upper airway cold receptors respectively, as first outlined by Eccles (2000). Figures 10.3 and 10.4 present updated models of menthol’s effects upon oral and upper airway cold receptors, using evidence presented in this thesis (Chapters 5-9). In this subsection, the outcome variables, thirst and ventilation will be discussed, along with the potential consideration of hydration status. The potential role of habituation to menthol mouth swilling has been discussed in sections 10.2.2.1 and 10.2.2.3.

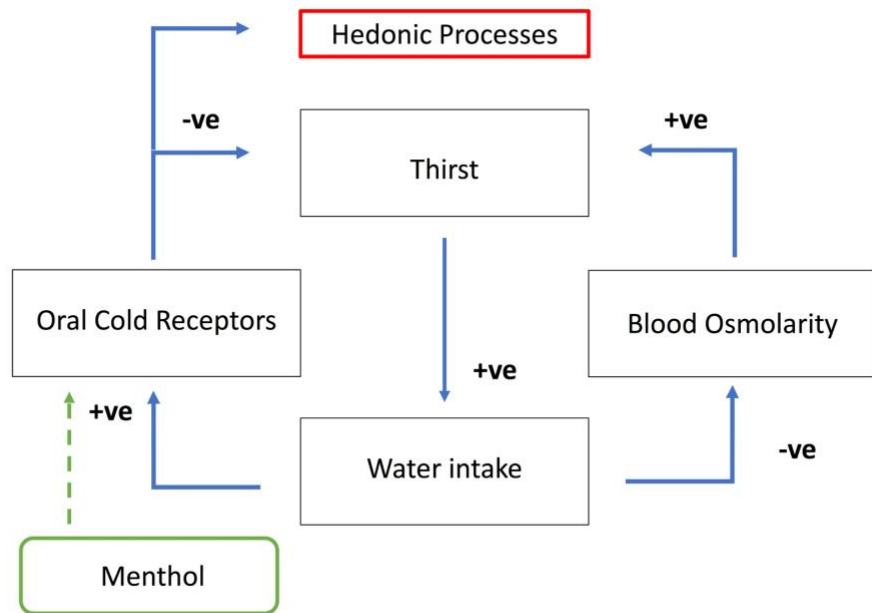


Figure 10-1 Effects of menthol application upon thirst and associated factors as per Eccles (2000)

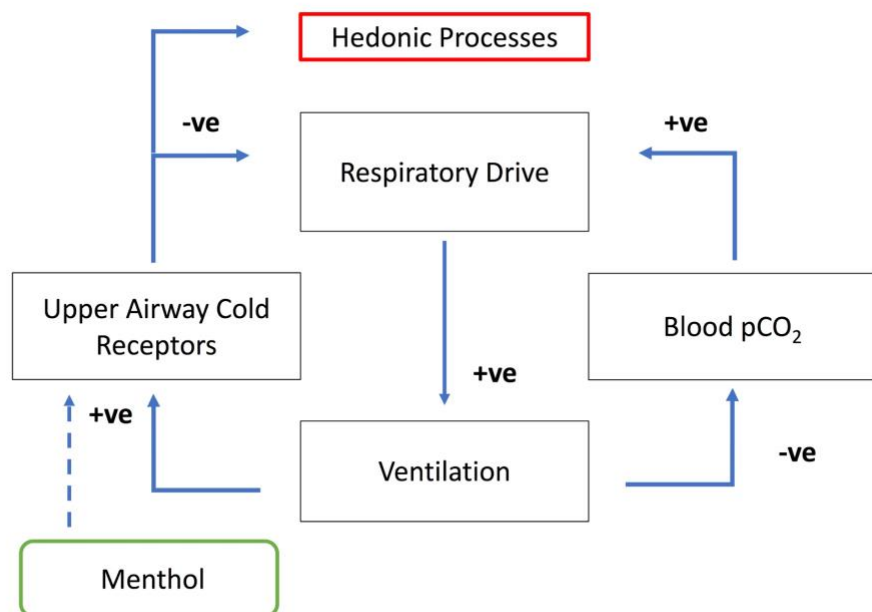


Figure 10-2 Effects of menthol application upon ventilation and associated factors as per Eccles (2000)

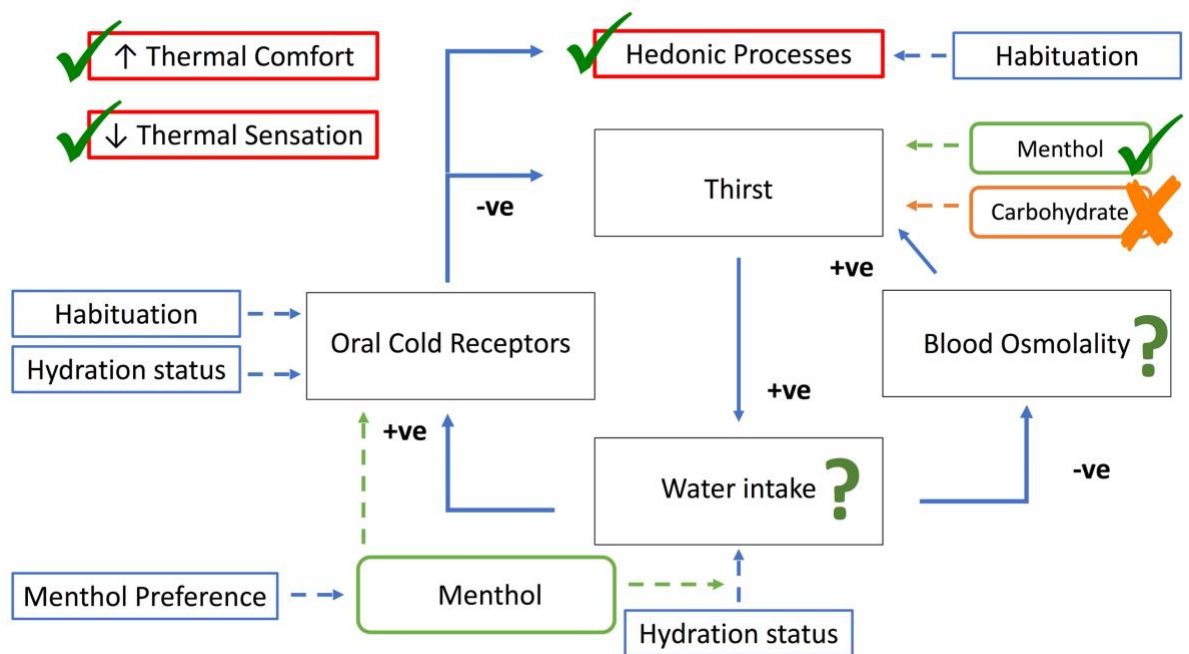


Figure 10-3 Effects of menthol application upon thirst and associated factors updated to include the findings of this thesis, other works and proposed future routes of investigation.

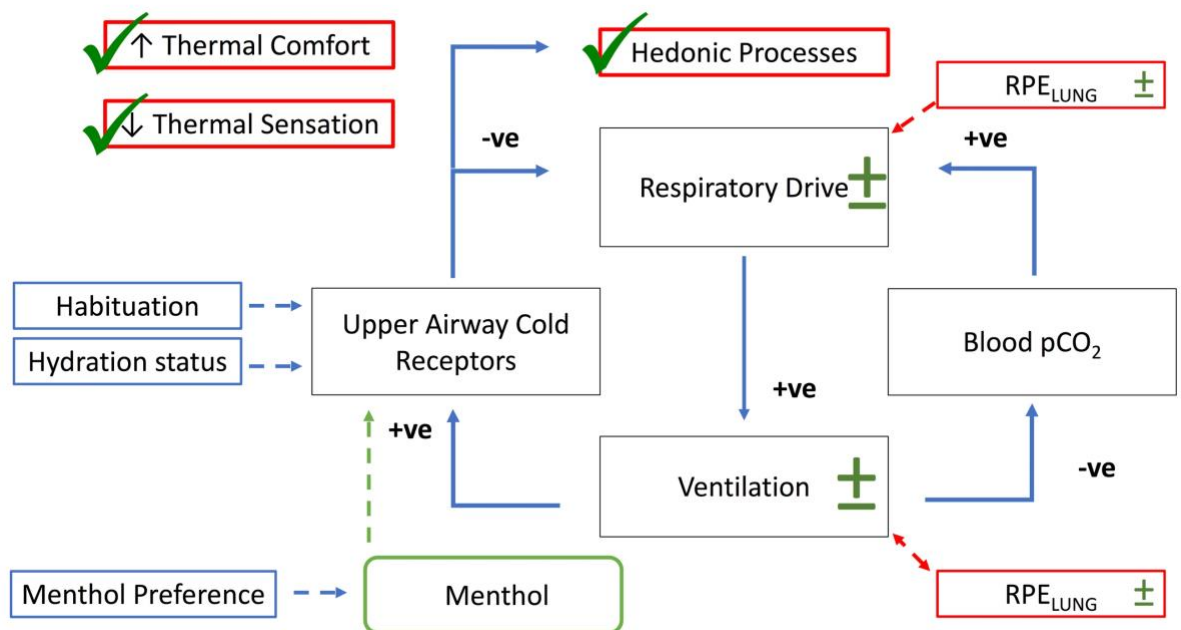


Figure 10-4 Effects of menthol application upon ventilation, updated to include the findings of this thesis and future considerations

Thirst was assessed throughout Chapters 6 – 8 of this thesis; both at rest and during exercise. The rationale for this was twofold: firstly, thirst provides valuable homeostatic information when exercising under hot conditions, and secondly menthol has previously been reported, as expressed by the models above, to satiate thirst (Eccles, 2000; Eccles *et al.*, 2013). Importantly, as defined by Epstein (1991), thirst is best represented ‘as a motivational state of readiness to consume water’ (Epstein, 1991) and is not simply

drinking behaviour, but the drive that provokes this response and is accompanied by hedonic experiences upon satiation (Epstein, 1991; Eccles, 2000). Physiological, transient states such as a 'dry mouth' may correlate to an increase in thirst but are not considered robust indicators of thirst in and of themselves.

At rest in a hot environment in non-heat acclimated individuals (Chapter 6) we found menthol to be a water mimetic, and thus was capable of satiating thirst as well as water and exceeding carbohydrate's ability to do so. Typical reductions in thirst were found to be -0.92 ± 0.25 and -0.57 ± 0.25 arbitrary units with respect to a no swill control and carbohydrate swill (*moderate* differences). Greater variation in thirst responses was seen during exercise (Chapters 7 and 8), this may be attributed in part to the perceived respiratory load imposed by the exercise, especially at higher running velocities (Chapter 7), or during continuous exercise (Chapter 8).

Ventilatory responses to exercise and menthol mouth swilling also displayed variation in this thesis, but did trend upwards with increased running speed (Chapter 7), and as exercise duration progressed when expressed relative to physiological cooling (Ice; Chapter 8). These findings somewhat mirror the trends observed with thirst, and suggest that menthol induced increases in $\dot{V}E$, may indeed promote thirst due to an increased flow of air brought about by a suppressed respiratory drive as per Figures 10.1 and 10.3.

In the athletes in the chapters which assessed exercise performance, an increase in $\dot{V}E$ may have been perceived as inhibitory to their performance, as increased $\dot{V}E$ requires an increased tidal volume and or respiratory frequency, which may be accountable for an increase in RPE_{lung} , which was also synonymous with higher running speeds in menthol conditions. However, heat was a greater driver of $\dot{V}E$ in this investigation than menthol mouth swilling, suggesting that well-trained athletes are more responsive to temperature, than to temperature mimetics i.e. they require greater input to alter oral cold perception and so attenuate RPE_{lung} and thirst. This may suggest that the greater the training status of an athlete, the more potent the perceptual cooling stimulus needed to produce a desired effect. If so, combined physiological and perceptual strategies such as those employed by Riera and colleagues (Riera *et al.*, 2014; Tran Trong *et al.*, 2015; Riera *et al.*, 2016) may meet this demand.

The potential role of hydration status is highlighted in Figures 10.1 and 10.3, as expressed by blood osmolality. In hindsight, hydration status can be easily assessed upon arrival to the laboratory, via refractometry, specific gravity or a urine colour chart (Armstrong, 2007; McKenzie, Munoz and Armstrong, 2015), and may have been a fascinating covariate in the analyses undertaken within this thesis. Blood osmolality is affected by water intake

which is provoked by thirst. This thesis has shown that menthol mouth swilling can directly influence thirst and as such investigating the potential role of hydration status as it affects menthol's efficacy as an ergogenic aid is warranted. This may take place either pre-experiment via manipulations in percentage bodyweight loss before undertaking exercise (graded hypohydration), or by assessing per- and post-exercise fluid intake following menthol mouth swilling.

10.2.3.3 Timing of application

The timing of menthol application in relation to exercise has typically followed a regular pattern with researchers using time or distance completed to prescribe application intervals in the oral literature, and pre-exercise or continuous application, through use of a soaked garment for example, being most common in the topical literature.

Details of research conducted to date are noted in the table below (Table 10.1), and are categorised by method of application (oral and topical), and sub-categorised by exercise protocol. For completeness, topical literature is also included, as topical application of menthol also targets TRPM8 receptors, but the thickness of the stratum corneum at the site of application will be thicker than that of the oral cavity (H.R. Watson *et al.*, 1978). Topical literature also employs a different frequency of application to menthol mouth swilling literature, which demonstrates greater feasibility as a percooling strategy, compared to the pre-exercise timing employed in topical investigations.

If one calculates an average *N* of menthol exposures via oral application it approaches five applications per bout, irrespective of timing. This repeated approach presents a consistent stimulus to the oral cavity and may serve to regularly reset or refresh the trigeminal sensation, and subsequent interpretation of temperature. Performance is therefore improved because the environmental temperature is perceived as less deleterious (i.e. perceptual cooling), and may be accompanied by reductions in thermal sensation, and / or improvements in thermal comfort. However, most recently Jeffries *et al.*, (2018) demonstrated that the administration of a single menthol mouth swill at 85% of previously attained TTE, improved performance to a practically meaningful extent (Jeffries, Goldsmith and Waldron, 2018). This suggests that a more nuanced application of menthol mouth swilling during the bout may be warranted, provided that it is employed in line with a previously established physiological or performance construct.

In contrast, topical application takes place prior to the exercise bout, typically in a single exposure (Table 10.1). Repeated topical applications have taken place (Barwood, Kupusarevic and Goodall, 2018), but the potential impracticality of implementing such a

strategy during competition was acknowledged by the authors (Barwood, Kupusarevic and Goodall, 2018). Continuous applications through a menthol-soaked garment may present a sensory overload of sorts, whereby an athlete is either desensitised to the menthol stimulus due to saturation of TRPM8 receptors, or irritation and pain occur.

When the timings of topical and oral application of menthol mouth swilling are presented collectively, it may be the presentation of a novel TRPM8 stimulus that proves ergogenic, as opposed to menthol having a directly ergogenic effect. This suggests that menthol is disruptive as opposed to directly ergogenic, but can still be effective in enhancing performance, especially when timed appropriately relative to fatigue. A randomised investigation into different menthol ‘feeding strategies’ may in part confirm this notion. However, the number of trials required to explore all possibilities would most likely be impractical. Figure 10.5 below depicts some intervals that researchers may wish to consider as a starting point, but is not exhaustive (58 possible trial combinations in total). A grid such as this may be useful for either future research design, or strategizing the implementation of menthol containing strategies during supported competitions.


















	Start	0km	7.5km	15km	22.5km	30km	37.5km	40km
A								End
B								End
C								End
D								End
E								End
F								End

Figure 10-5 Schematic representing a variety of time points for menthol mouth swill administration (green cup) during a 40km cycling time trial. Example A represents a starting dose, much like topical literature. B represents a half way dose; C a 75% timing, similar to that of Jeffries et al., (2018). D denotes a 1/3 and 2/3 strategy. E is a start, third and two thirds dose (per 15km completed) and F is similar to E, but with a delayed start interval.

Table 10-1 Research designs and the frequency and number of exposures of menthol employed in oral and topical applications of menthol, to date. Please note (Botonis et al., 2016) is not included as the exercise portion of the trial preceded menthol application; (Akehi and Long, 2013) and (Topp, Ledford and Jacks, 2013) were excluded due to the passive nature of the exercise and menthol exposure, with (Topp et al., 2011) focusing upon strength outcomes and so sitting outside of the scope of this synthesis. Abbreviations: CWI: Cold Water Immersion; TTE: Time to Exhaustion; TT: Time Trial; N: number of menthol applications. Definition: Continuous is used to describe a timing that takes place for the entire exercise bout, due to menthol being applied to a garment or directly to the individual's skin for the entirety of the exercise bout.

Oral Application					
<i>Design</i>	<i>Author</i>	<i>Exercise Modality</i>	<i>Menthol %</i>	<i>Timing</i>	<i>N</i>
<i>Intermittent</i>	Gibson <i>et al.</i> , (2018)	Cycling	0.01%	Every 10 min i.e. fifth sprint	4
<i>Time to Exhaustion</i>	Flood <i>et al.</i> , (2017)	Cycling	0.01%	10 min intervals	Participant dependent
	Jeffries <i>et al.</i> , (2018)	Cycling	0.01%	85% TTE	1
	Mündel & Jones (2010)	Cycling	0.01%	10 min intervals	Participant dependent
<i>Time Trial</i>	Riera <i>et al.</i> , (2014)	Cycling	0.01%	Every 7.5km during TT	5
	Riera <i>et al.</i> , (2016)	Cycling	0.025%	Pre, Post Warm up; every 5km during TT	6
	Stevens <i>et al.</i> , (2016)	Running	0.01%	Every 5 min during preload; every km during TT	8
	Stevens <i>et al.</i> , (2017)	Running	0.01%	Every km during TT	5
	Tran Trong <i>et al.</i> , (2015)	Simulated Triathlon	0.025%	During run block (5 x 4km cycling + 1km run)	5

Topical Application					
<i>Design</i>	<i>Author</i>	<i>Exercise Modality</i>	<i>Menthol concentration</i>	<i>Frequency of application</i>	<i>N</i>
<i>Fixed Duration</i>	Bright <i>et al.</i> , (2018)	Cycling	4%	Every 20 min during exercise	5 (maximum)
	Gillis <i>et al.</i> , (2010)	Cycling	0.05% or 0.2%	Pre-exercise	1
	Gillis <i>et al.</i> , (2015)	Cycling	0.05% or 0.2%	Pre-exercise	1
	Gillis <i>et al.</i> , (2016)	Stepping	0.2%	Continuous	1
	Rinaldi <i>et al.</i> , (2018)	Cycling	0.1%	In between bout CWI	1
<i>Fixed Temperature</i>	Kounalakis <i>et al.</i> , (2010)	Cycling	4.6%	Continuous	1
<i>Intermittent</i>	Gillis <i>et al.</i> , (2018)	Sprints	4.0%	Post exercise + 2 x day ⁻¹ for five days	11 (total)
<i>Time to Exhaustion</i>	Barwood <i>et al.</i> , (2018)	Cycling	0.20%	At 20 min & 40 min	2
<i>Time Trial</i>	Barwood <i>et al.</i> , (2012)	Cycling	0.05%	Continuous	1
	Barwood <i>et al.</i> , (2014)	Running	0.20%	Continuous	1

10.3 Conclusion

The work presented in this thesis documented the development and application of a mentholated solution in trained middle and long distance runners, at intensities representative of training and competition. Firstly, a thorough analysis of the effects of internal and external cooling methodologies applied before and during time trial performance and an accompanying examination of menthol application during and following exercise were conducted. These reviews demonstrated that internal application of cooling strategies across the exercise bout, and internal application of menthol are most likely to improve performance, respectively. Consequently, a novel menthol solution was created, refined and applied at rest and at progressive and fixed exercise intensities. At rest, alterations in thermal perceptual sensations consistent with literature were observed, especially providing empirical support to menthol's ability to alter thirst. During progressive exercise, responses showed a great deal of variability, possibly due to inter-individual differences in relative exercise intensities, especially in hot conditions. These individual responses to menthol swilling were also apparent during fixed intensity exercise, yet menthol induced moderate improvements in thermal comfort and thirst. Despite limited ergogenic effects noted in experimental studies, most likely due to athletes' training status, when asked to reflect upon their experiences, participants reflected positively upon their perceptions of menthol mouth swilling and expressed a desire for the strategy to be available outside of the confines of the laboratory.

CHAPTER 11 : REFERENCES

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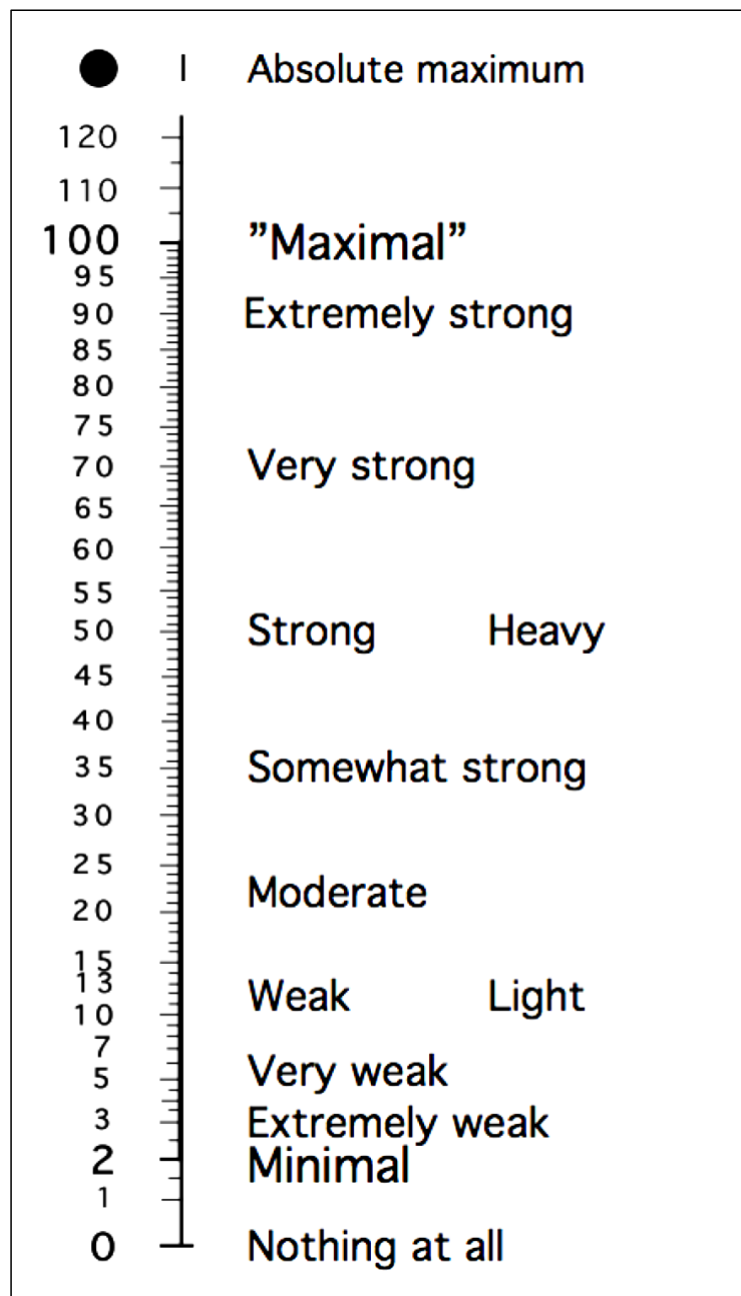
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CHAPTER 12 : APPENDICES

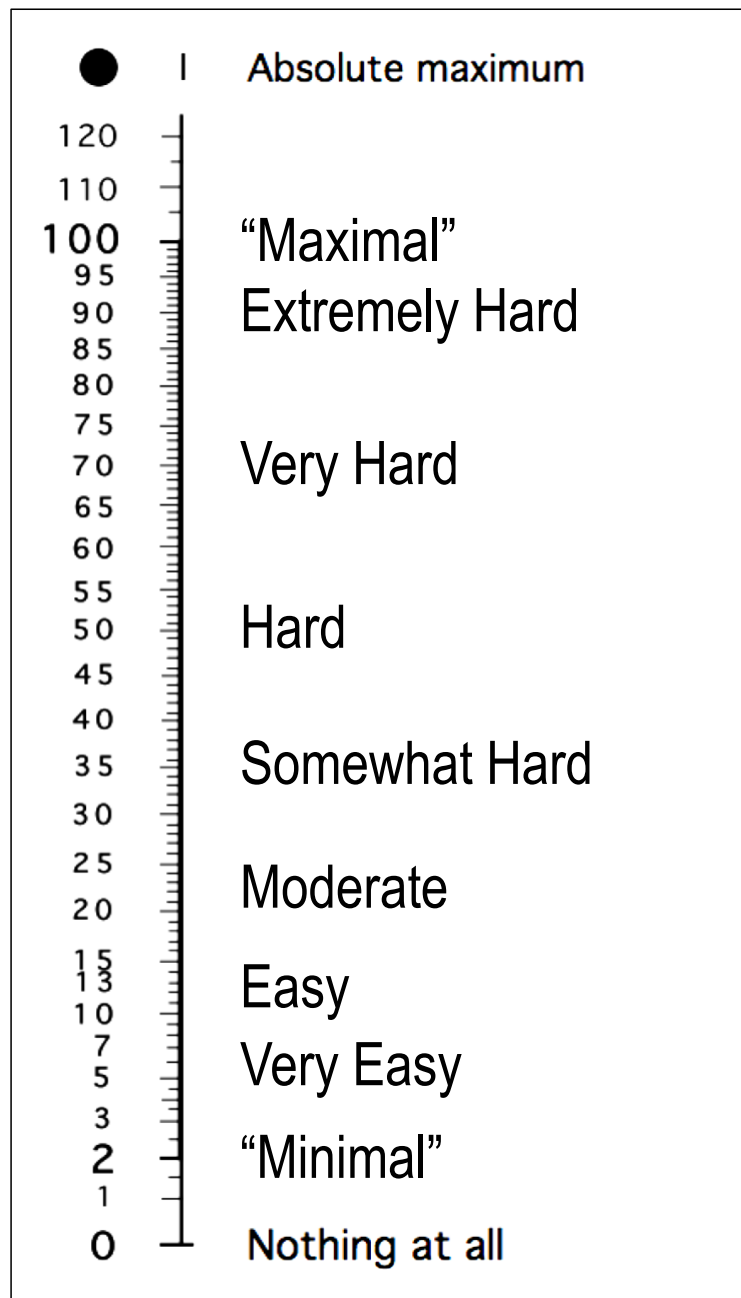
Appendix 1: CR100 scale of perceived exertion

Original Scale



(E. Borg and G. Borg 2002)

Idiomatic English Verbal Descriptors



(E. Borg and G. Borg, 2002)

Very Hot	4
Hot	3
Warm	2
Slightly Warm	1
Neutral	0
Slightly Cool	-1
Cool	-2
Cold	-3
Very cold	-4

Please describe how hot you feel now

(Zhang *et al.*, 2004)

Very Comfortable	4
	3
Comfortable	2
	1
Just comfortable	+0
Just uncomfortable	-0
	-1
Uncomfortable	-2
	-3
Very Uncomfortable	-4

Please describe how comfortable you feel now

(Zhang *et al.*, 2004)

Appendix 3: Thirst Scale

Severely Thirsty	9
	8
	7
	6
	5
	4
	3
	2
	1
Not at all thirsty	0

(Engell *et al.*, 1987)